FIGURE 1

PANEL A

PANEL B

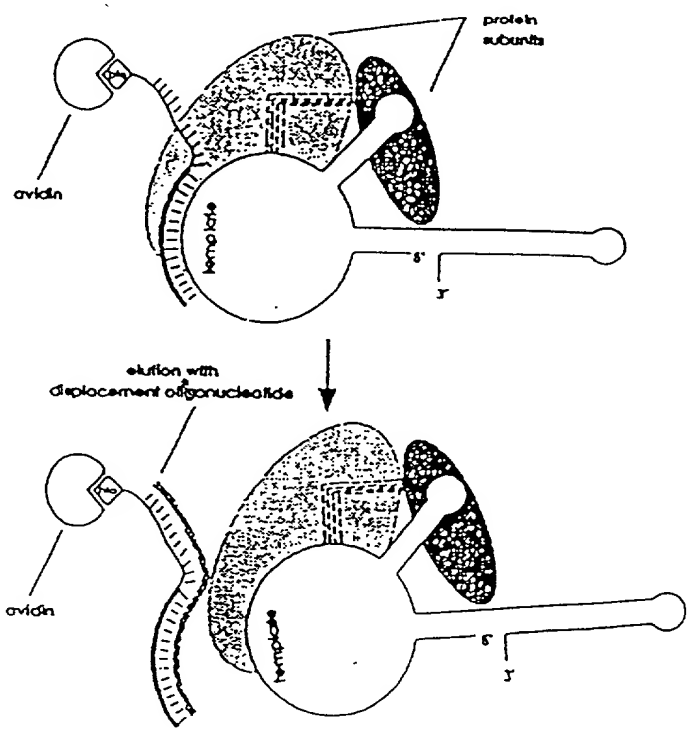

FIGURE 2

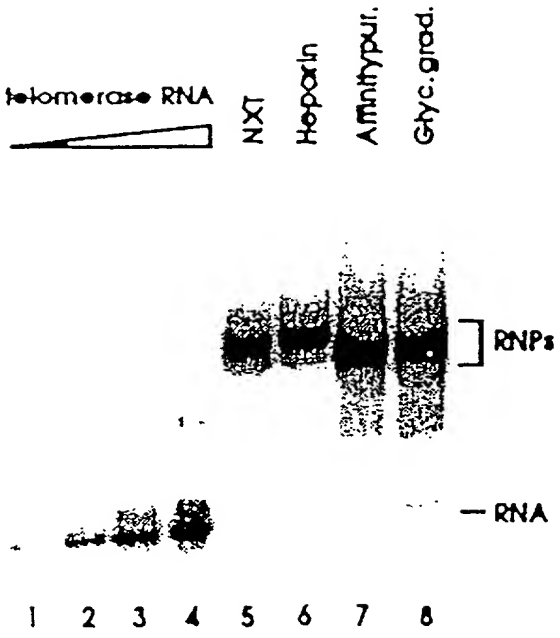
telomerase RNA
NXT
Heparin
Affinitypur.
Glyc.grad.
RNPs
RNA
1 2 3 4 5 6 7 8

FIGURE 3

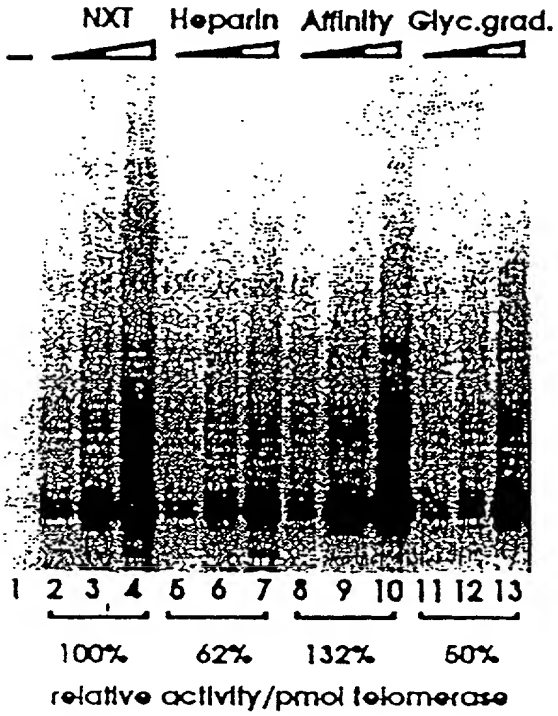
NXT
Heparin
Affinity
Glyc.grad.
1 2 3 4 5 6 7 8 9 10 11 12 13
100%
62%
132%
50%
relative activity/pmol telomerase

FIGURE 4

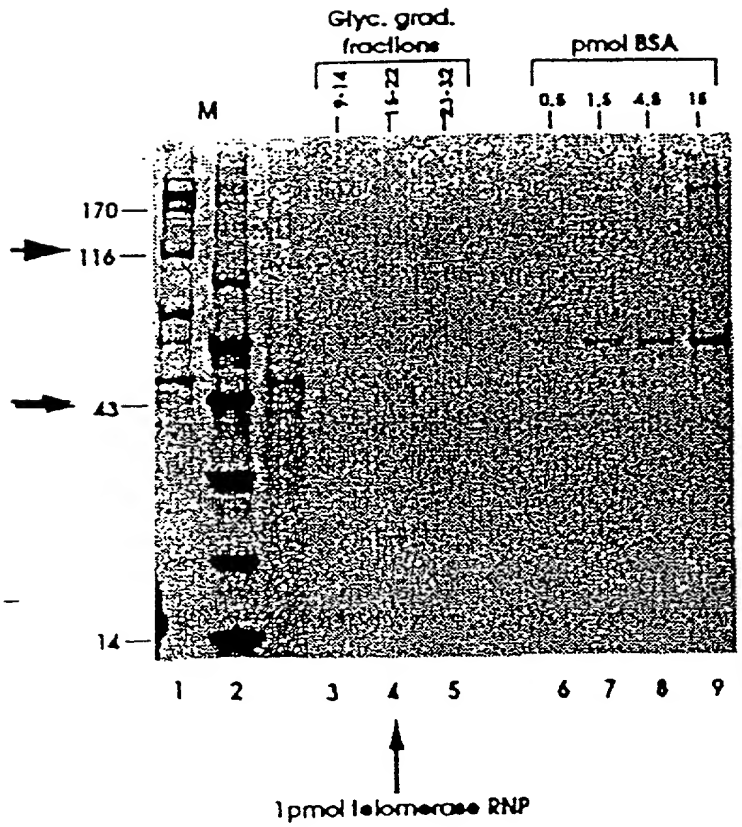
Glyc. grad. fractions
pmol BSA
M
0.5
1.5
4.5
15
170
116
43
14
1
2
3
4
5
6
7
8
9
1pmol telomerase RNP

FIGURE 5

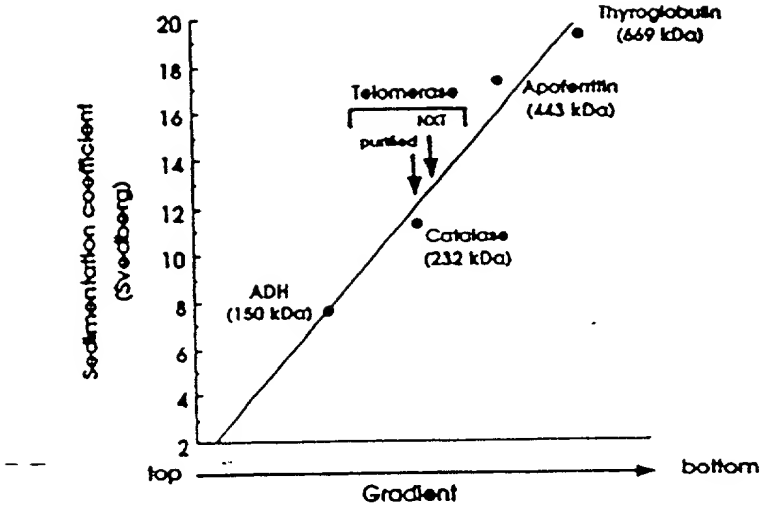
Thyroglobulin
(669 kDa)
Telomerase
RNT
purified
Apoferritin
(443 kDa)
Catalase
(232 kDa)
ADH
(150 kDa)
Sedimentation coefficient
(Svedberg)
20
18
16
14
12
10
8
6
4
2
top
bottom
Gradient

FIGURE 6

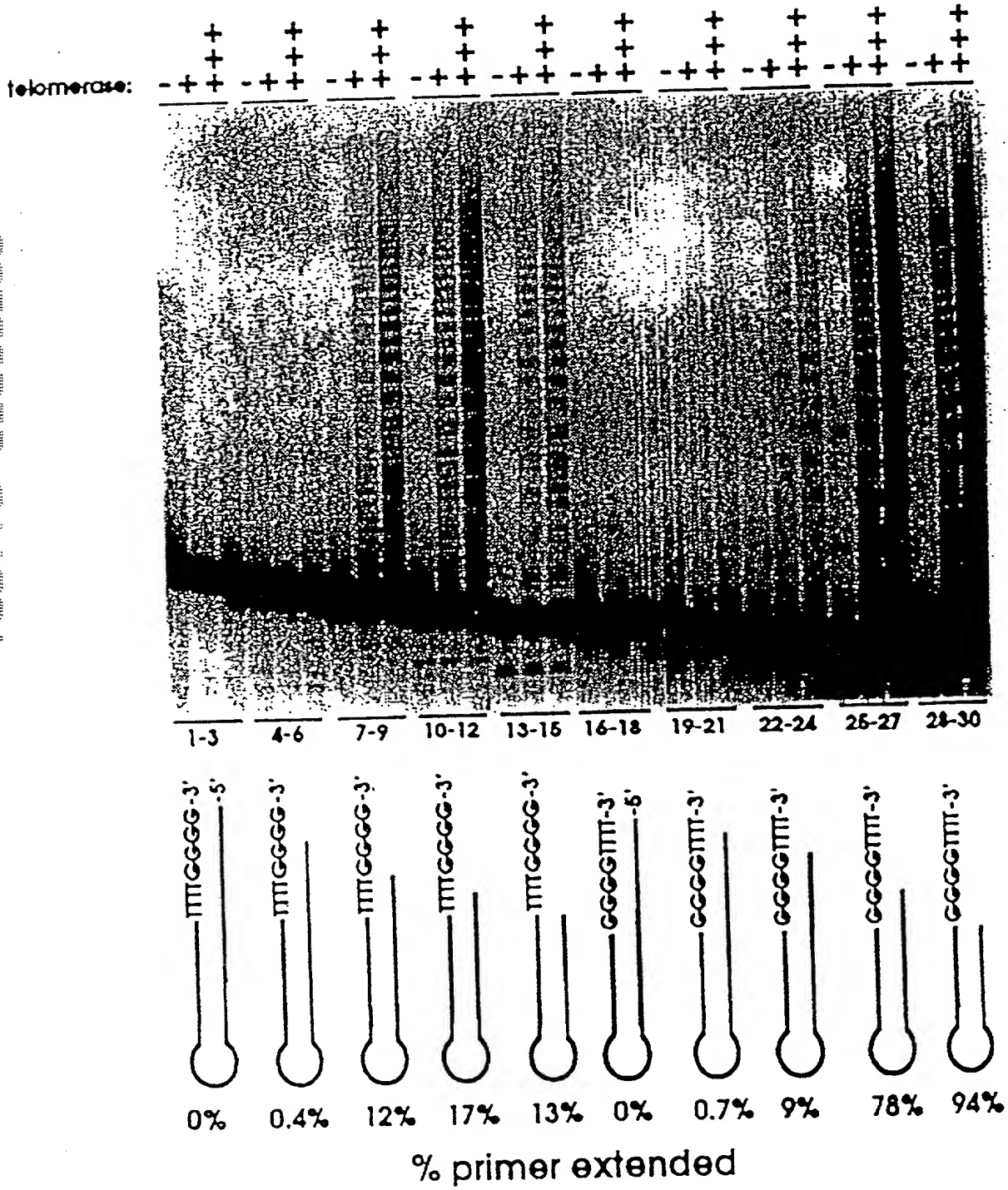
telomerase:
- + + - + + - + + - + + - + + - + + - + + - + + - + + - + +
1-3
4-6
7-9
10-12
13-15
16-18
19-21
22-24
25-27
28-30
TTAGGG-3'
5'
TTAGGG-3'
TTAGGG-3'
TTAGGG-3'
TTAGGG-3'
GGGTTA-3'
6'
GGGTTA-3'
GGGTTA-3'
GGGTTA-3'
GGGTTA-3'
0%
0.4%
12%
17%
13%
0%
0.7%
9%
78%
94%
% primer extended

FIGURE 7

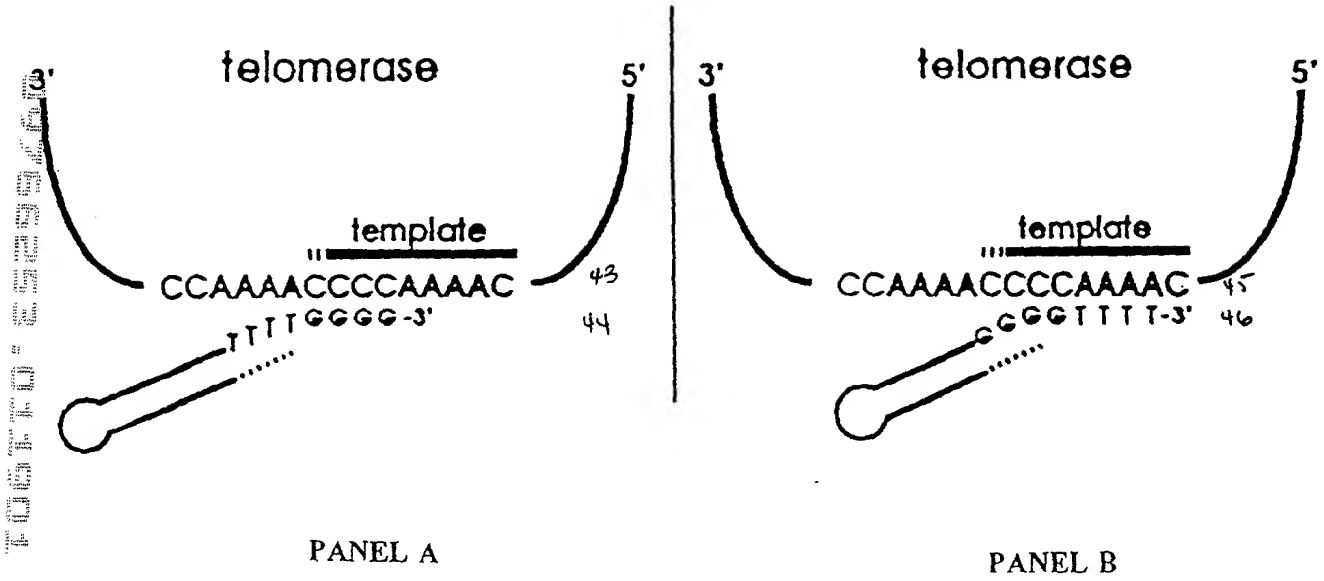
3'
telomerase
5'
template
CCAAAACCCCAAAAC
TTTTGGGG-3'
43
44
PANEL A
3'
telomerase
5'
template
CCAAAACCCCAAAAC
GGGTTTT-3'
45
46
PANEL B

FIGURE 8

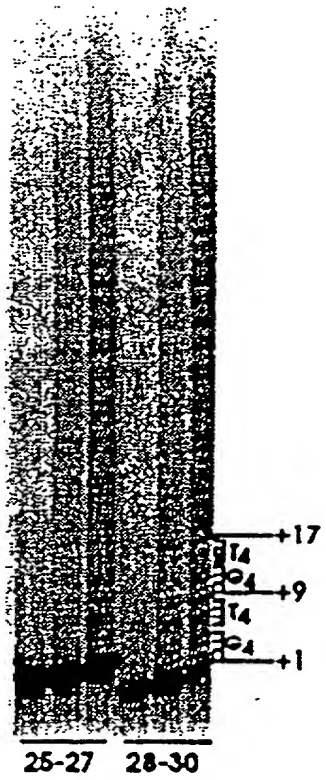

FIGURE 9

```
   1 AAAACCCCAA AACCCCAAAA CCCCTTTTAG AGCCCTGCAG TTGGAAATAT
  51 AACCTCAGTA TTAATAAGCT CAGATTTTAA ATATTAATTA CAAAACCTAA
 101 ATGGAGGTTG ATGTTGATAA TCAAGCTGAT AATCATGGCA TTCACTCAGC
 151 TCTTAAGACT TGTGAAGAAA TTAAAGAAGC TAAAACGTTG TACTCTTGGA
 201 TCCAGAAAGT TATTAGATGA AGAAATCAAT CTCAAAGTCA TTATAAAGAT
 251 TTAGAAGATA TTAAAATATT TGCGCAGACA AATATTGTTG CTACTCCACG
 301 AGACTATAAT GAAGAAGATT TTAAAGTTAT TGCAAGAAAA GAAGTATTTT
 351 CAACTGGACT AATGATCGAA CTTATTGACA AATGCTTAGT TGAACTTCTT
 401 TCATCAAGCG ATGTTTCAGA TAGACAAAAA CTTCAATGAT TTGGATTTCA
 451 ACTTAAGGGA AATCAATTAG CAAAGACCCA TTTATTAACA GCTCTTTCAA
 501 CTCAAAAGCA GTATTTCTTT CAAGACGAAT GGAACCAAGT TAGAGCAATG
 551 ATTGGAAATG AGCTCTTCCG ACATCTCTAC ACTAAATATT TAATATTCCA
 601 GCGAACTTCT GAAGGAACTC TTGTTCAATT TTGCGGGAAT AACGTTTTTG
 651 ATCATTTGAA AGTCAACGAT AAGTTTGACA AAAAGCAAAA AGGTGGAGCA
 701 GCAGACATGA ATGAACCTCG ATGTTGATCA ACCTGCAAAT ACAATGTCAA
 751 GAATGAGAAA GATCACTTTC TCAACAACAT CAACGTGCCG AATTGGAATA
 801 ATATGAAATC AAGAACCAGA ATATTTTATT GCACTCATTT TAATAGAAAT
 851 AACCAATTCT TCAAAAAGCA TGAGTTTGTG AGTAACAAAA ACAATATTTC
 901 AGCGATGGAC AGAGCTCAGA CGATATTCAC GAATATATTC AGATTTAATA
 951 GAATTAGAAA GAAGCTAAAA GATAAGGTTA TCGAAAAAAT TGCCTACATG
1001 CTTGAGAAAG TCAAAGATTT TAACTTCAAC TACTATTTAA CAAAATCTTG
1051 TCCTCTTCCA GAAAATTGGC GGGAACGGAA ACAAAAAAATC GAAAACTTGA
1101 TAAATAAAAC TAGAGAAGAA AAGTCGAAGT ACTATGAAGA GCTGTTTAGC
1151 TACACAACTG ATAATAAATG CGTCACACAA TTTATTAATG AATTTTTCTA
1201 CAATATACTC CCCAAAGACT TTTTGACTGG AAGAAACCGT AAGAATTTTC
1251 AAAAGAAAGT TAAGAAATAT GTGGAACTAA ACAAGCATGA ACTCATTCAC
1301 AAAAACTTAT TGCTTGAGAA GATCAATACA AGAGAAATAT CATGGATGCA
1351 GGTTGAGACC TCTGCAAAGC ATTTTTATTA TTTTGATCAC GAAAACATCT
1401 ACGTCTTATG GAAATTGCTC CGATGGATAT TCGAGGATCT CGTCGTCTCG
1451 CTGATTAGAT GATTTTTCTA TGTCACCGAG CAACAGAAAA GTTACTCCAA
1501 AACCTATTAC TACAGAAAGA ATATTTGGGA CGTCATTATG AAAATGTCAA
1551 TCGCAGACTT AAAGAAGGAA ACGCTTGCTG AGGTCCAAGA AAAAGAGGTT
1601 GAAGAATGGA AAAAGTCGCT TGGATTTGCA CCTGGAAAAC TCAGACTAAT
1651 ACCGAAGAAA ACTACTTTCC GTCCAATTAT GACTTTCAAT AAGAAGATTG
1701 TAAATTCAGA CCGGAAGACT ACAAAATTAA CTACAAATAC GAAGTTATTG
1751 AACTCTCACT TAATGCTTAA GACATTGAAG AATAGAATGT TTAAAGATCC
1801 TTTTGGATTC GCTGTTTTTA ACTATGATGA TGTAATGAAA AAGTATGAGG
1851 AGTTTGTTTG CAAATGGAAG CAAGTTGGAC AACCAAAACT CTTCTTTGCA
1901 ACTATGGATA TCGAAAAGTG ATATGATAGT GTAAACAGAG AAAAACTATC
1951 AACATTCCTA AAAACTACTA AATTACTTTC TTCAGATTTC TGGATTATGA
2001 CTGCACAAAT TCTAAAGAGA AAGAATAACA TAGTTATCGA TTCGAAAAAC
2051 TTTAGAAAGA AAGAAATGAA AGATTATTTT AGACAGAAAT TCCAGAAGAT
2101 TGCACTTGAA GGAGGACAAT ATCCAACCTT ATTCAGTGTT CTTGAAAATG
2151 AACAAAATGA CTTAAATGCA AAGAAAACAT TAATTGTTGA AGCAAAGCAA
2201 AGAAATTATT TTAAGAAAGA TAACTTACTT CAACCAGTCA TTAATATTTG
2251 CCAATATAAT TACATTAACT TTAATGGGAA GTTTTATAAA CAAACAAAAG
2301 GAATTCCTCA AGGTCTTTGA GTTTCATCAA TTTTGTCATC ATTTTATTAT
```

FIGURE 9 (cont.)

2351 GCAACATTAG AGGAAAGCTC CTTAGGATTC CTTAGAGATG AATCAATGAA
2401 CCCTGAAAAT CCAAATGTTA ATCTTCTAAT GAGACTTACA GATGACTATC
2451 TTTTGATTAC AACTCAAGAG AATAATGCAG TATTGTTTAT TGAGAAACTT
2501 ATAAACGTAA GTCGTGAAAA TGGATTTAAA TTCAATATGA AGAAACTACA
2551 GACTAGTTTT CCATTAAGTC CAAGCAAATT TGCAAAATAC GGAATGGATA
2601 GTGTTGAGGA GCAAAATATT GTTCAAGATT ACTGCGATTG GATTGGCATC
2651 TCAATTGATA TGAAAACTCT TGCTTTAATG CCAAATATTA ACTTGAGAAT
2701 AGAAGGAATT CTGTGTACAC TCAATCTAAA CATGCAAACA AAGAAAGCAT
2751 CAATGTGGCT CAAGAAGAAA CTAAAGTCGT TTTTAATGAA TAACATTACC
2801 CATTATTTTA GAAAGACGAT TACAACCGAA GACTTTGCGA ATAAAACTCT
2851 CAACAAGTTA TTTATATCAG GCGGTTACAA ATACATGCAA TGAGCCAAAG
2901 AATACAAGGA CCACTTTAAG AAGAACTTAG CTATGAGCAG TATGATCGAC
2951 TTAGAGGTAT CTAAAATTAT ATACTCTGTA ACCAGAGCAT TCTTTAAATA
3001 CCTTGTGTGC AATATTAAGG ATACAATTTT TGGAGAGGAG CATTATCCAG
3051 ACTTTTTCCT TAGCACACTG AAGCACTTTA TTGAAATATT CAGCACAAAA
3101 AAGTACATTT TCAACAGAGT TTGCATGATC CTCAAGGCAA AAGAAGCAAA
3151 GCTAAAAAAGT GACCAATGTC AATCTCTAAT TCAATATGAT GCATAGTCGA
3201 CTATTCTAAC TTATTTTGGA AAGTTAATTT TCAATTTTTG TCTTATATAC
3251 TGGGGTTTTG GGGTTTTGGG GTTTTGGGG

FIGURE 10

1 MEVDVDNQAD NHGIHSALKT CEEIKEAKTL YSWIQKVIRC RNQSQSHYKD
51 LEDIKIFAQT NIVATPRDYN EEDFKVIARK EVFSTGLMIE LIDKCLVELL
101 SSSDVSDRQK LQCFGFQLKG NQLAKTHLLT ALSTQKQYFF QDEWNQVRAM
151 IGNELFRHLY TKYLIFQRTS EGTLVQFCGN NVFDHLKVND KFDKKQKGGA
201 ADMNEPRCCS TCKYNVKNEK DHFLNNINVP NWNNMKSRTR IFYCTHFNRN
251 NQFFKKHEFV SNKNNISAMD RAQTIFTNIF RFNRIRKKLK DKVIEKIAYM
301 LEKVKDFNFN YYLTKSCPLP ENWRERKQKI ENLINKTREE KSKYYEELFS
351 YTTDNKCVTQ FINEFFYNIL PKDFLTGRNR KNFQKKVKKY VELNKHELIH
401 KNLLLEKINT REISWMQVET SAKHFYYFDH ENIYVLWKLL RWIFEDLVVS
451 LIRCFFYVTE QQKSYSKTYY YRKNIWDVIM KMSIADLKKE TLAEVQEKEV
501 EEWKKSLGFA PGKLRLIPKK TTFRPIMTFN KKIVNSDRKT TKLTTNTKLL
551 NSHLMLKTLK NRMFKDPFGF AVFNYDDVMK KYEEFVCKWK QVGQPKLFFA
601 TMDIEKCYDS VNREKLSTFL KTTKLLSSDF WIMTAQILKR KNNIVIDSKN
651 FRKKEMKDYF RQKFQKIALE GGQYPTLFSV LENEQNDLNA KKTLIVEAKQ
701 RNYFKKDNLL QPVINICQYN YINFNGKFYK QTKGIPQGLC VSSILSSFYY
751 ATLEESSLGF LRDESMNPEN PNVNLLMRLT DDYLLITTQE NNAVLFIEKL
801 INVSRENGFK FNMKKLQTSF PLSPSKFAKY GMDSVEEQNI VQDYCDWIGI
851 SIDMKTLALM PNINLRIEGI LCTLNLNMQT KKASMWLKKK LKSFLMNNIT
901 HYFRKTITTE DFANKTLNKL FISGGYKYMQ CAKEYKDHFK KNLAMSSMID
951 LEVSKIIYSV TRAFFKYLVC NIKDTIFGEE HYPDFFLSTL KHFIEIFSTK
1001 KYIFNRVCMI LKAKEAKLKS DQCQSLIQYD A

FIGURE 11

```
   1 CCCCAAAACC CCAAAACCCC AAAACCCCTA TAAAAAAAGA AAAAATTGAG
  51 GTAGTTTAGA AATAAAATAT TATTCCCGCA CAAATGGAGA TGGATATTGA
 101 TTTGGATGAT ATAGAAAATT TACTTCCTAA TACATTCAAC AAGTATAGCA
 151 GCTCTTGTAG TGACAAGAAA GGATGCAAAA CATTGAAATC TGGCTCGAAA
 201 TCGCCTTCAT TGACTATTCC AAAGTTGCAA AAACAATTAG AGTTCTACTT
 251 CTCGGATGCA AATCTTTATA ACGATTCTTT CTTGAGAAAA TTAGTTTTAA
 301 AAAGCGGAGA GCAAAGAGTA GAAATTGAAA CATTACTAAT GTTTAAATAA
 351 AATCAGGTAA TGAGGATTAT TCTATTTTTT AGATCACTTC TTAAGGAGCA
 401 TTATGGAGAA AATTACTTAA TACTAAAAGG TAAACAGTTT GGATTATTTC
 451 CCTAGCCAAC AATGATGAGT ATATTAAATT CATATGAGAA TGAGTCAAAG
 501 GATCTCGATA CATCAGACTT ACCAAAGACA AACTCGCTAT AAAACGCAAG
 551 AAAAAGTTTG ATAATCGAAC AGCAGAAGAA CTTATTGCAT TTACTATTCG
 601 TATGGGTTTT ATTACAATTG TTTTAGGTAT CGACGGTGAA CTCCCGAGTC
 651 TTGAGACAAT TGAAAAAGCT GTTTACAACT GAAGGAATCG CAGTTCTGAA
 701 AGTTCTGATG TGTATGCCAT TATTTTGTGA ATTAATCTCA AATATCTTAT
 751 CTCAATTTAA TGGATAGCTA TAGAAACAAA CCAAATAAAC CATGCAAGTT
 801 TAATGGAATA TACGTTAAAT CCTTTGGGAC AAATGCACAC TGAATTTATA
 851 TTGGATTCTT AAAGCATAGA TACACAGAAT GCTTTAGAGA CTGATTTAGC
 901 TTACAACAGA TTACCTGTTT TGATTACTCT TGCTCATCTC TTATATCTTT
 951 AAAAGAAGCA GGCGAAATGA AAAGAAGACT AAAGAAAGAG ATTTCAAAAT
1001 TTGTTGATTC TTCTGTAACC GGAATTAACA ACAAGAATAT TAGCAACGAA
1051 AAAGAAGAAG AGCTATCACA ATCCTGATTC TTAAAGATTT CAAAAATTCC
1101 AGGTAAGAGA GATACATTCA TTAAAATTCA TATATTATAG TTTTTCATTT
1151 CACAGCTGTT ATTTTCTTTT ATCTTAACAA TATTTTTTGA TTAGCTGGAA
1201 GTAAAAAGTA TCAAATAAGA GAAGCGCTAG ACTGAGGTAA CTTAGCTTAT
1251 TCACATTCAT AGATCGACCT TCATATATCC AATACGATGA TAAGGAAACA
1301 GCAGTCATCC GTTTTAAAAA TAGTGCTATG AGGACTAAAT TTTTAGAGTC
1351 AAGAAATGGA GCCGAAATCT TAATCAAAAA GAATTGCGTC GATATTGCAA
1401 AAGAATCGAA CTCTAAATCT TTCGTTAATA AGTATTACCA ATCTTGATTG
1451 ATTGAAGAGA TTGACGAGGC AACTGCACAG AAGATCATTA AAGAAATAAA
1501 GTAACTTTTA TTAATTAGAG AATAAACTAA ATTACTAATA TAGAGATCAG
1551 CGATCTTCAA TTGACGAAAT AAAAGCTGAA CTAAAGTTAG ACAATAAAAA
1601 ATACAAACCT TGGTCAAAAT ATTGAGGAAG GAAAAGAAGA CCAGTTAGCA
1651 AAAGAAAAAA TAAGGCAATA AATAAAATGA GTACAGAAGT GAAGAAATAA
1701 AAGATTTATT TTTTTCAATA ATTTATTGAA AAGAGGGGTT TTGGGGTTTT
1751 GGGGTTTTGG GG
```

FIGURE 12

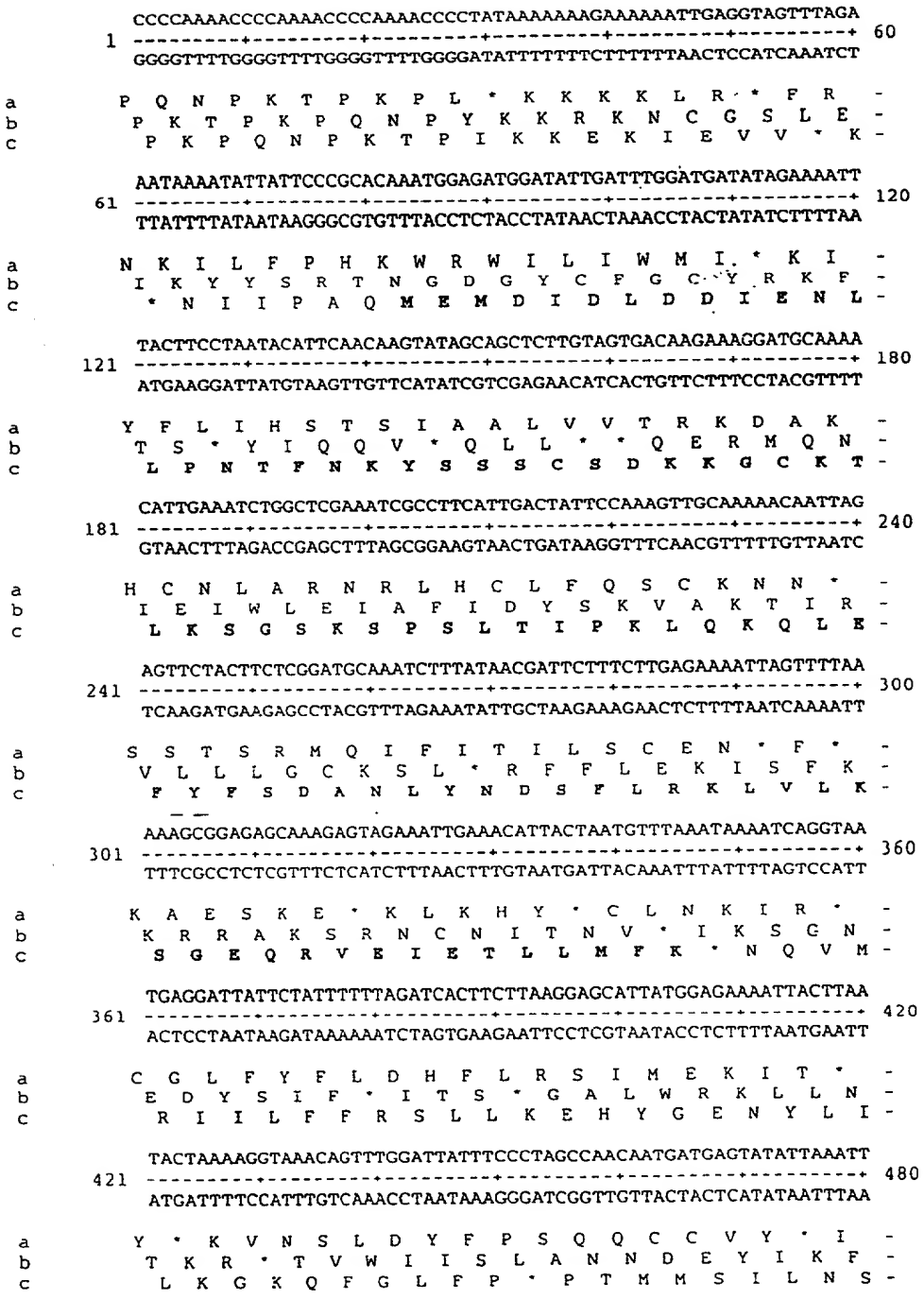
CCCCAAAACCCCAAAACCCCAAAACCCCTATAAAAAAAGAAAAAATTGAGGTAGTTTAGA
1
60
GGGGTTTTGGGGTTTTGGGGTTTTGGGGATATTTTTTTCTTTTTTAACTCCATCAAATCT
a P Q N P K T P K P L * K K K K L R * F R -
b P K T P K P Q N P Y K K R K N C G S L E -
c P K P Q N P K T P I K K E K I E V V * K -
AATAAAATATTATTCCCGCACAAATGGAGATGGATATTGATTTGGATGATATAGAAAATT
61
120
TTATTTTATAATAAGGGCGTGTTTACCTCTACCTATAACTAAACCTACTATATCTTTTAA
a N K I L F P H K W R W I L I W M I * K I -
b I K Y Y S R T N G D G Y C F G C Y R K F -
c * N I I P A Q M E M D I D L D D I E N L -
TACTTCCTAATACATTCAACAAGTATAGCAGCTCTTGTAGTGACAAGAAAGGATGCAAAA
121
180
ATGAAGGATTATGTAAGTTGTTCATATCGTCGAGAACATCACTGTTCTTTCCTACGTTTT
a Y F L I H S T S I A A L V V T R K D A K -
b T S * Y I Q Q V * Q L L * * Q E R M Q N -
c L P N T F N K Y S S S C S D K K G C K T -
CATTGAAATCTGGCTCGAAATCGCCTTCATTGACTATTCCAAAGTTGCAAAAACAATTAG
181
240
GTAACTTTAGACCGAGCTTTAGCGGAAGTAACTGATAAGGTTTCAACGTTTTTGTTAATC
a H C N L A R N R L H C L F Q S C K N N * -
b I E I W L E I A F I D Y S K V A K T I R -
c L K S G S K S P S L T I P K L Q K Q L E -
AGTTCTACTTCTCGGATGCAAATCTTTATAACGATTCTTTCTTGAGAAAATTAGTTTTAA
241
300
TCAAGATGAAGAGCCTACGTTTAGAAATATTGCTAAGAAAGAACTCTTTTAATCAAAATT
a S S T S R M Q I F I T I L S C E N * F * -
b V L L L G C K S L * R F F L E K I S F K -
c F Y F S D A N L Y N D S F L R K L V L K -
AAAGCGGAGAGCAAAGAGTAGAAATTGAAACATTACTAATGTTTAAATAAAATCAGGTAA
301
360
TTTCGCCTCTCGTTTCTCATCTTTAACTTTGTAATGATTACAAATTTATTTTAGTCCATT
a K A E S K E * K L K H Y * C L N K I R * -
b K R R A K S R N C N I T N V * I K S G N -
c S G E Q R V E I E T L L M F K * N Q V M -
TGAGGATTATTCTATTTTTTAGATCACTTCTTAAGGAGCATTATGGAGAAAATTACTTAA
361
420
ACTCCTAATAAGATAAAAAATCTAGTGAAGAATTCCTCGTAATACCTCTTTTAATGAATT
a C G L F Y F L D H F L R S I M E K I T * -
b E D Y S I F * I T S * G A L W R K L L N -
c R I I L F F R S L L K E H Y G E N Y L I -
TACTAAAAGGTAAACAGTTTGGATTATTTCCCTAGCCAACAATGATGAGTATATTAAATT
421
480
ATGATTTTCCATTTGTCAAACCTAATAAAGGGATCGGTTGTTACTACTCATATAATTTAA
a Y * K V N S L D Y F P S Q Q C C V Y * I -
b T K R * T V W I I S L A N N D E Y I K F -
c L K G K Q F G L F P * P T M M S I L N S -

FIGURE 12 (cont.)

```
     CATATGAGAATGAGTCAAAGGATCTCGATACATCAGACTTACCAAAGACAAACTCGCTAT
 481 ---------+---------+---------+---------+---------+---------+ 540
     GTATACTCTTACTCAGTTTCCTAGAGCTATGTAGTCTGAATGGTTTCTGTTTGAGCGATA

a    H  M  R  M  S  Q  R  I  S  I  H  Q  T  Y  Q  R  Q  T  R  Y  -
b     I  C  E  C  V  K  G  S  R  Y  I  R  L  T  K  D  K  L  A  I -
c      Y  E  N  E  S  K  D  L  D  T  S  D  L  P  K  T  N  S  L  * -

     AAAACGCAAGAAAAAGTTTGATAATCGAACAGCAGAAGAACTTATTGCATTTACTATTCG
 541 ---------+---------+---------+---------+---------+---------+ 600
     TTTTGCGTTCTTTTTCAAACTATTAGCTTGTCGTCTTCTTGAATAACGTAAATGATAAGC

a    K  T  Q  E  K  V  C  *  S  N  S  R  R  T  Y  C  I  Y  Y  S  -
b     K  R  K  K  K  F  D  N  R  T  A  E  E  L  I  A  F  T  I  R -
c      N  A  R  K  S  L  I  I  E  Q  Q  K  N  L  L  H  L  L  F  V -

     TATGGGTTTTATTACAATTGTTTTAGGTATCGACGGTGAACTCCCGAGTCTTGAGACAAT
 601 ---------+---------+---------+---------+---------+---------+ 660
     ATACCCAAAATAATGTTAACAAAATCCATAGCTGCCACTTGAGGGCTCAGAACTCTGTTA

a    Y  G  F  Y  Y  N  C  F  R  Y  R  R  C  T  P  E  S  C  D  N  -
b     M  G  F  I  T  I  V  L  G  I  D  G  E  L  P  S  L  E  T  I -
c      W  V  L  L  Q  L  F  *  V  S  T  V  N  S  R  V  L  R  Q  L -

     TGAAAAAGCTGTTTACAACTGAAGGAATCGCAGTTCTGAAAGTTCTGATGTGTATGCCAT
 661 ---------+---------+---------+---------+---------+---------+ 720
     ACTTTTTCGACAAATGTTGACTTCCTTAGCGTCAAGACTTTCAAGACTACACATACGGTA

a    C  K  S  C  L  Q  L  K  E  S  Q  F  C  K  F  *  C  V  C  H  -
b     E  K  A  V  Y  N  C  R  N  R  S  S  E  S  S  D  V  Y  A  I -
c      K  K  L  F  T  T  E  G  I  A  V  L  K  V  L  M  C  M  P  L -

     TATTTTGTGAATTAATCTCAAATATCTTATCTCAATTTAATGGATAGCTATAGAAACAAA
 721 ---------+---------+---------+---------+---------+---------+ 780
     ATAAAACACTTAATTAGAGTTTATAGAATAGAGTTAAATTACCTATCGATATCTTTGTTT

a    Y  F  V  N  *  S  Q  I  S  Y  L  N  L  M  D  S  Y  R  N  K  -
b     I  L  C  I  N  L  K  Y  L  I  S  I  *  W  I  A  I  E  T  N -
c      F  C  E  L  I  S  N  I  L  S  Q  F  N  G  *  L  *  K  Q  T -

     CCAAATAAACCATGCAAGTTTAATGGAATATACGTTAAATCCTTTGGGACAAATGCACAC
 781 ---------+---------+---------+---------+---------+---------+ 840
     GGTTTATTTGGTACGTTCAAATTACCTTATATGCAATTTAGGAAACCCTGTTTACGTGTG

a    P  N  K  P  C  K  F  N  G  I  Y  V  K  S  F  G  T  N  A  H  -
b     Q  I  N  H  A  S  L  M  E  Y  T  L  N  P  L  G  Q  M  H  T -
c      K  *  T  M  Q  V  *  W  N  I  R  *  I  L  W  D  K  C  T  L -

     TGAATTTATATTGGATTCTTAAAGCATAGATACACAGAATGCTTTAGAGACTGATTTAGC
 841 ---------+---------+---------+---------+---------+---------+ 900
     ACTTAAATATAACCTAAGAATTTCGTATCTATGTGTCTTACGAAATCTCTGACTAAATCG

a    C  I  Y  I  G  F  L  K  H  R  Y  T  E  C  F  R  D  C  F  S  -
b     E  F  I  L  D  S  *  S  I  D  T  Q  N  A  L  E  T  D  L  A -
c      N  L  Y  W  I  L  K  A  *  I  H  R  M  L  *  R  L  I  *  L -

     TTACAACAGATTACCTGTTTTGATTACTCTTGCTCATCTCTTATATCTTTAAAAGAAGCA
 901 ---------+---------+---------+---------+---------+---------+ 960
     AATGTTGTCTAATGGACAAAACTAATGAGAACGAGTAGAGAATATAGAAATTTTCTTCGT

a    L  Q  Q  I  T  C  F  D  Y  S  C  S  S  L  I  S  L  K  E  A  -
b     Y  N  R  L  P  V  L  I  T  L  A  H  L  L  Y  L  *  K  K  Q -
c      T  T  D  Y  L  F  C  L  L  L  L  I  S  Y  I  F  K  R  S  R -

     GGCGAAATGAAAAGAAGACTAAAGAAAGAGATTTCAAAATTTGTTGATTCTTCTGTAACC
 961 ---------+---------+---------+---------+---------+---------+ 1020
     CCGCTTTACTTTTCTTCTGATTTCTTTCTCTAAAGTTTTAAACAACTAAGAAGACATTGG

a    G  E  M  K  R  R  L  K  K  E  I  S  K  F  V  D  S  S  V  T  -
b     A  K  C  K  E  D  *  R  K  R  F  Q  N  L  L  I  L  L  *  P -
c      R  N  E  K  K  T  K  E  R  D  F  K  I  C  C  F  F  C  N  R -

     GGAATTAACAACAAGAATATTAGCAACGAAAAAGAAGAAGAGCTATCACAATCCTGATTC
1021 ---------+---------+---------+---------+---------+---------+ 1080
     CCTTAATTGTTGTTCTTATAATCGTTGCTTTTTCTTCTTCTCGATAGTGTTAGGACTAAG

a    G  I  N  N  K  N  I  S  N  E  K  E  E  E  L  S  Q  S  C  F  -
b     E  L  T  T  R  I  L  A  T  K  K  K  K  S  Y  H  N  P  D  S -
c      N  *  Q  Q  E  Y  *  Q  R  K  R  R  R  A  I  T  I  L  I  L -
```

FIGURE 12 (cont.)

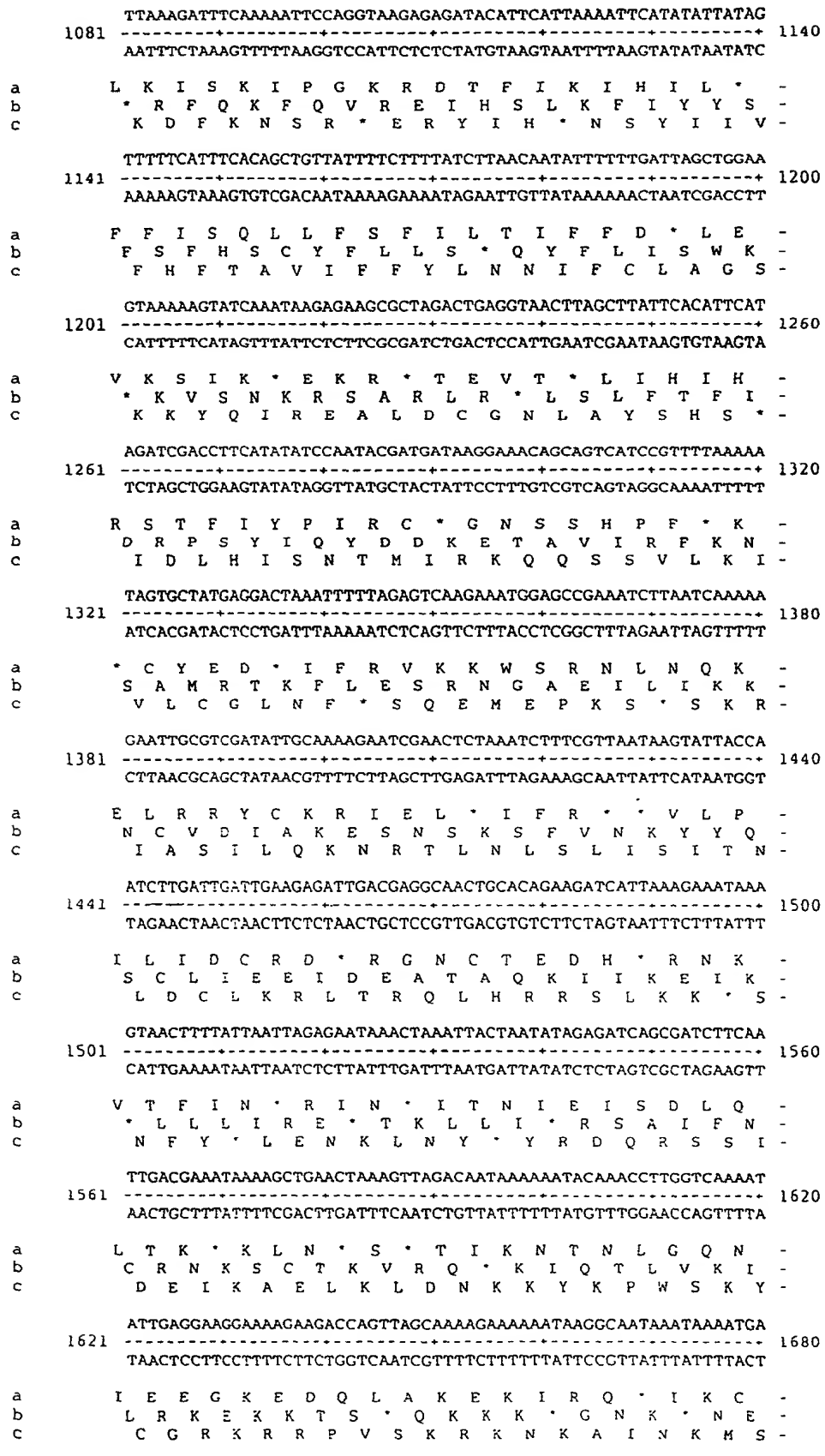

FIGURE 12 (cont.)

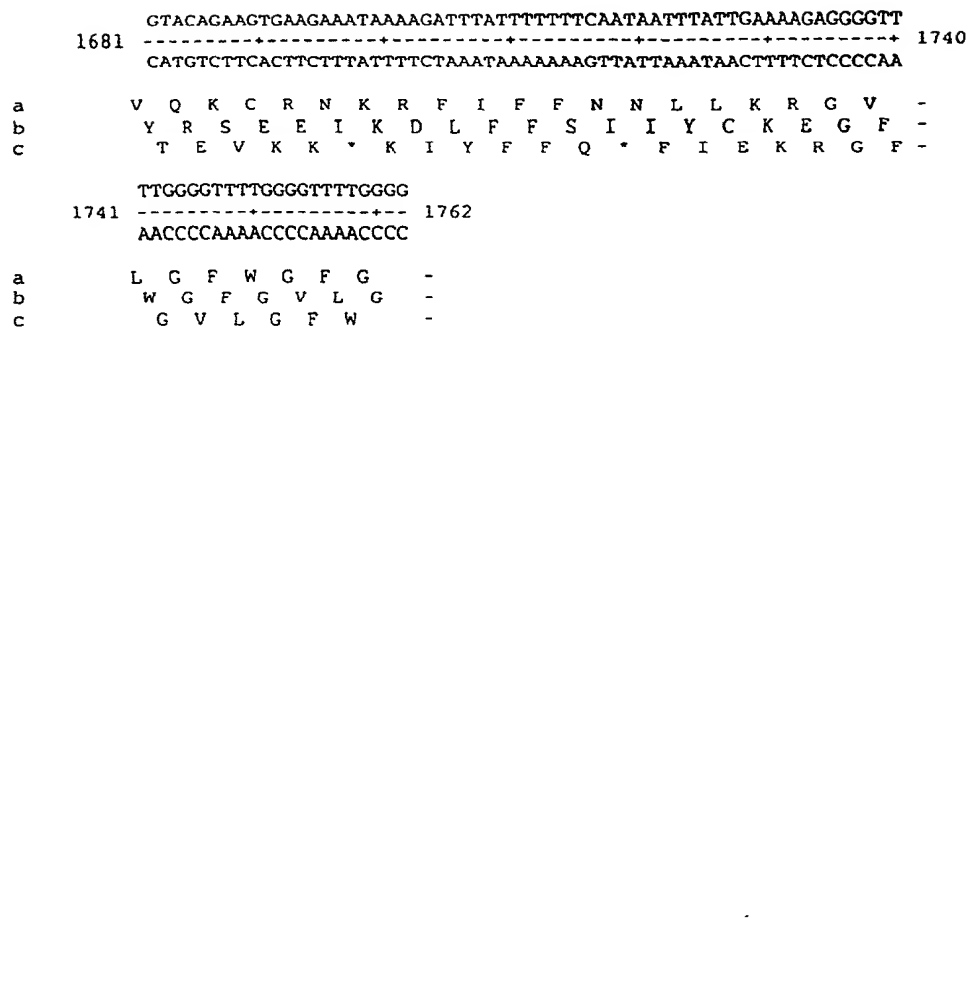

FIGURE 13

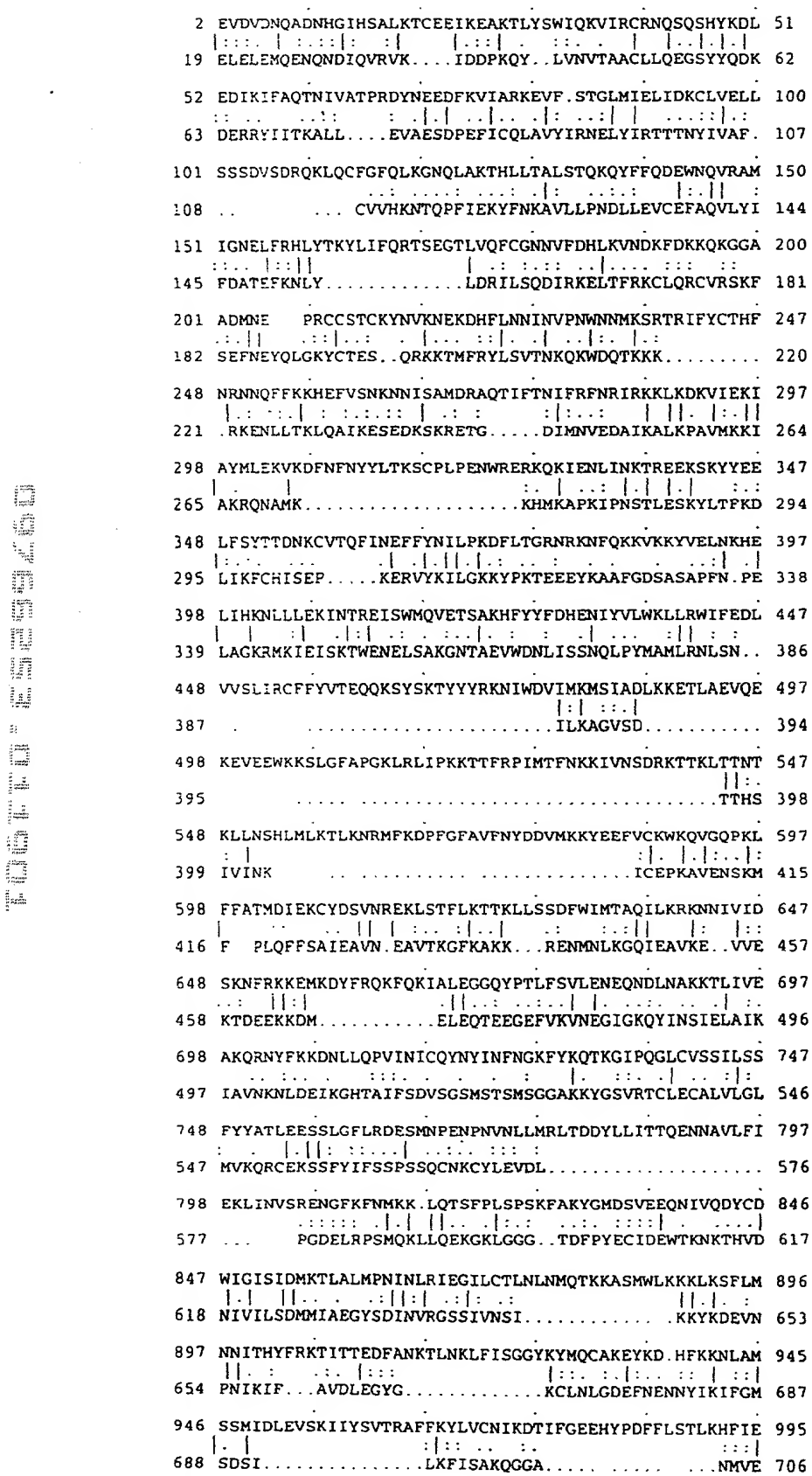

FIGURE 14

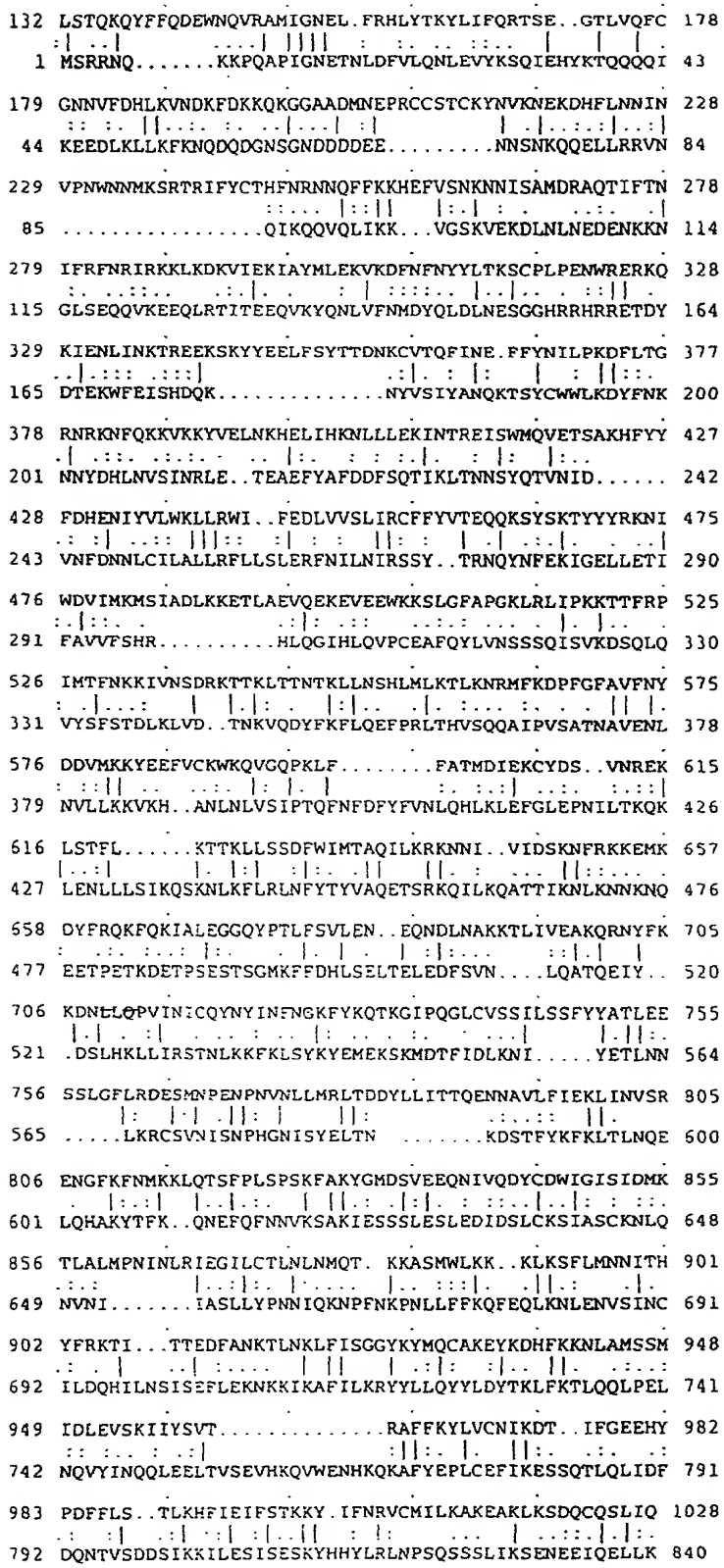
132 LSTQKQYFFQDEWNQVRAMIGNEL.FRHLYTKYLIFQRTSE..GTLVQFC 178
1 MSRRNQ.....KKPQAPIGNETNLDFVLQNLEVYKSQIEHYKTQQQQI 43
179 GNNVFDHLKVNDKFDKKQKGGAADMNEPRCCSTCKYNVKNEKDHFLNNIN 228
44 KEEDLKLLKFKNQDQDGNSGNDDDEE.....NNSNKQQELLRRVN 84
229 VPNWNNMKSRTRIFYCTHFNRNNQFFKKHEFVSNKNNISAMDRAQTIFTN 278
85 .....QIKQQVQLIKK...VGSKVEKDLNLNEDENKKN 114
279 IFRFNRIRKKLKDKVIEKIAYMLEKVKDFNFNYYLTKSCPLPENWRERKQ 328
115 GLSEQQVKEEQLRTITEEQVKYQNLVFNMDYQLDLNESGGHRRHRRETDY 164
329 KIENLINKTREEKSKYYEELFSYTTDNKCVTQFINE.FFYNILPKDFLTG 377
165 DTEKWFEISHDQK.....NYVSIYANQKTSYCWWLKDYFNK 200
378 RNRKNFQKKVKKYVELNKHELIHKNLLLEKINTREISWMQVETSAKHFYY 427
201 NNYDHLNVSINRLE..TEAEFYAFDDFSQTIKLTNNSYQTVNID..... 242
428 FDHENIYVLWKLLRWI..FEDLVVSLIRCFFYVTEQQKSYSKTYYYRKNI 475
243 VNFDNNLCILALLRFLLSLERFNILNIRSSY..TRNQYNFEKIGELLETI 290
476 WDVIMKMSIADLKKETLAEVQEKEVEEWKKSLGFAPGKLRLIPKKTTFRP 525
291 FAVVFSHR.....HLQGIHLQVPCEAFQYLVNSSSQISVKDSQLQ 330
526 IMTFNKKIVNSDRKTTKLTTNTKLLNSHLMLKTLKNRMFKDPFGFAVFNY 575
331 VYSFSTDLKLVD..TNKVQDYFKFLQEFPRLTHVSQQAIPVSATNAVENL 378
576 DDVMKKYEEFVCKWKQVGQPKLF.....FATMDIEKCYDS..VNREK 615
379 NVLLKKVKH..ANLNLVSIPTQFNFDFYFVNLQHLKLEFGLEPNILTKQK 426
616 LSTFL.....KTTKLLSSDFWIMTAQILKRKNNI..VIDSKNFRKKEMK 657
427 LENLLLSIKQSKNLKFLRLNFYTYVAQETSRKQILKQATTIKNLKNNKNQ 476
658 DYFRQKFQKIALEGGQYPTLFSVLEN..EQNDLNAKKTLIVEAKQRNYFK 705
477 EETPETKDETPSESTSGMKFFDHLSELTELEDFSVN....LQATQEIY.. 520
706 KDNLLQPVINICQYNYINFNGKFYKQTKGIPQGLCVSSILSSFYYATLEE 755
521 .DSLHKLLIRSTNLKKFKLSYKYEMEKSKMDTFIDLKNI.....YETLNN 564
756 SSLGFLRDESMNPENPNVNLLMRLTDDYLLITTQENNAVLFIEKLINVSR 805
565 .....LKRCSVNISNPHGNISYELTN .....KDSTFYKFKLTLNQE 600
806 ENGFKFNMKKLQTSFPLSPSKFAKYGMDSVEEQNIVQDYCDWIGISIDMK 855
601 LQHAKYTFK..QNEFQFNNVKSAKIESSSLESLEDIDSLCKSIASCKNLQ 648
856 TLALMPNINLRIEGILCTLNLNMQT. KKASMWLKK..KLKSFLMNNITH 901
649 NVNI.....IASLLYPNNIQKNPFNKPNLLFFKQFEQLKNLENVSINC 691
902 YFRKTI...TTEDFANKTLNKLFISGGYKYMQCAKEYKDHFKKNLAMSSM 948
692 ILDQHILNSISEFLEKNKKIKAFILKRYYLLQYYLDYTKLFKTLQQLPEL 741
949 IDLEVSKIIYSVT.....RAFFKYLVCNIKDT..IFGEEHY 982
742 NQVYINQQLEELTVSEVHKQVWENHKQKAFYEPLCEFIKESSQTLQLIDF 791
983 PDFFLS..TLKHFIEIFSTKKY.IFNRVCMILKAKEAKLKSDQCQSLIQ 1028
792 DQNTVSDDSIKKILESISESKYHHYLRLNPSQSSSLIKSENEEIQELLK 840

FIGURE 15

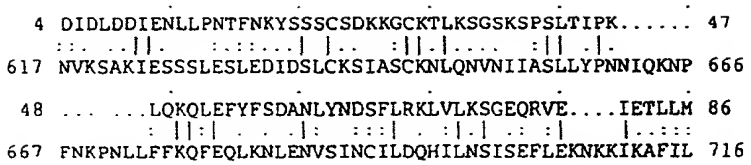
4 DIDLDDIENLLPNTFNKYSSSCSDKKGCKTLKSGSKSPSLTIPK..... 47
617 NVKSAKIESSSLESLEDIDSLCKSIASCKNLQNVNIIASLLYPNNIQKNP 666
48 ... ...LQKQLEFYFSDANLYNDSFLRKLVLKSGEQRVE....IETLLM 86
667 FNKPNLLFFKQFEQLKNLENVSINCILDQHILNSISEFLEKNKKIKAFIL 716

FIGURE 16

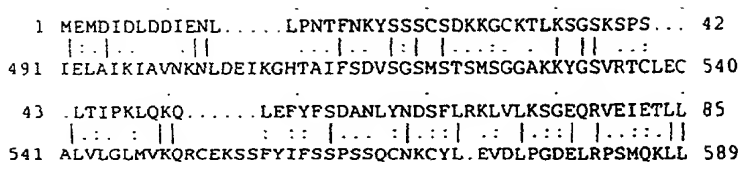
1 MEMDIDLDDIENL.....LPNTFNKYSSSCSDKKGCKTLKSGSKSPS... 42
491 IELAIKIAVNKNLDEIKGHTAIFSDVSGSMSTSMSGGAKKYGSVRTCLEC 540
43 .LTIPKLQKQ.....LEFYFSDANLYNDSFLRKLVLKSGEQRVEIETLL 85
541 ALVLGLMVKQRCEKSSFYIFSSPSSQCNKCYL.EVDLPGDELRPSMQKLL 589

FIGURE 17

```
                                Motif A                                                Motif B
                           h--hDh---h--h                                        h---+-QG---SP
Consensus
telomerase p123  GQPKLFFATMDIEKCYDSVNREKLSTFLKTTKLL-100-KFYKQTKGIPQGLCVSSILSSFYYATLEESSLGFL
Dong (LINE)      KNRNLHCTYIDYKKAFDSIPHSWLIQVLEIYKIN-  28-RQIAIKKGIYQGDSLSPLWFCLALNPLSHQLHNDR
al S.c.(groupII) FGGSNWFREVDLKKCFDTISHDLIIKELKRYISD-  26-HVPVGPRVCVQGAPTSPALCNAVLLRLDRRLAGLA
HIV-RT           LKKKKSVTVLDVGDAYFSVPLDEDFRKYTAFTIP-   7-GIRYQYNVLPQGWKGSPAIFQSSMTKILEPFRKQN
L8543.12 yeast   VLPELYFMKFDVKSCYDSIPRMECMRILKDALKN-  68-KCYIREDGLFQGSSLSAPIVDLVYDDLLEFYSEFK

                            Motif C                                    Motif D           Motif E
                        h--YhDDhhh                                   Gh-h---K           h-hLGh-h
Consensus
telomerase p123  -14-LMRLTDDYLLITTQENN-0-AVLFIEKLINVSRENGFKFNMKKLQT-23-QDYCDWIGISI
Dong (LINE)      -16-HLIYMDDIKLYAKNDKE-0-MKKLIDTTTIFSNDISMQFGLDKCKT-25-KCLYKYLGFQQ
al S.c.(groupII) -55-YVRYADDILIGVLGSKN-2-KIIKRDLNNFLNS.LGLTINEEKTLI- 4-ETPARFLGYNI
HIV-RT           - 4-IYQYMDDLYVGSHLEIG-1-HRTKIEELRQHLLRWGLTTPDKKHQK- 0-EPPFLWMGYEL
L8543.12 yeast   - 8-ILKLADDFLIISTDQQQ.......VINIKKLAMGGFQKYNAKANR-41-IRSKSSKGIFR
```

FIGURE 18

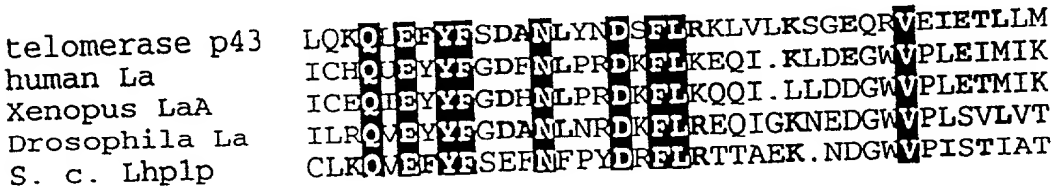
telomerase p43
human La
Xenopus LaA
Drosophila La
S. c. Lhp1p
LQKQLEFYFSDANLYNDSFLRKLVLKSGEQRVEIETLLM
ICHQLEYYFGDFNLPRDKFLKEQI.KLDEGWVPLEIMIK
ICEQLEYYFGDHNLPRDKFLKQQI.LLDDGWVPLETMIK
ILRQVEYYFGDANLNRDKFLREQIGKNEDGWVPLSVLVT
CLKQVEFYFSEFNFPYDRFLRTTAEK.NDGWVPISTIAT

FIGURE 19

```
   1 aactcattta attactaatt taatcaacaa gattgataaa aagcagtaaa taaaacccaa
  61 tagatttaat ttagaaagta tcaattgaaa aatggaaatt gaaaacaact aagcacaata
 121 gccaaaagcc gaaaaattgt ggtgggaact tgaattagag atgcaagaaa accaaaatga
 181 tatataagtt agggttaaga ttgacgatcc taagcaatat ctcgtgaacg tcactgcagc
 241 atgtttgttg taggaaggta gttactacta agataaagat gaaagaagat atatcatcac
 301 taaagcactt cttgaggtgg ctgagtctga tcctgagttc atctgctagt tggcagtcta
 361 catccgtaat gaactttaca tcagaactac cactaactac attgtagcat tttgtgttgt
 421 ccacaagaat actcaaccat tcatcgaaaa gtacttcaac aaagcagtac ttttgcctaa
 481 tgacttactg gaagtctgtg aatttgcata ggttctctat atttttgatg caactgaatt
 541 caaaaatttg tatcttgata ggatactttc ataagatatt cgtaaggaac tcactttccg
 601 taagtgttta caaagatgcg tcagaagcaa gttttctgaa ttcaacgaat actaacttgg
 661 taagtattgc actgaatcct aacgtaagaa aacaatgttc cgttacctct cagttaccaa
 721 caagtaaaag tgggattaaa ctaagaagaa gagaaaagag aatctcttaa ccaaacttta
 781 ggcaataaag gaatctgaag ataagtccaa gagagaaact ggagacataa tgaacgttga
 841 agatgcaatc aaggctttaa aaccagcagt tatgaagaaa atagccaaga gatagaatgc
 901 catgaagaaa cacatgaagg cacctaaaat tcctaactct accttggaat caaagtactt
 961 gaccttcaag gatctcatta agttctgcca tatttctgag cctaaagaaa gagtctataa
1021 gatccttggt aaaaaatacc ctaagaccga agaggaatac aaagcagcct ttggtgattc
1081 tgcatctgca cccttcaatc ctgaattggc tggaaagcgt atgaagattg aaatctctaa
1141 aacatgggaa aatgaactca gtgcaaaagg caacactgct gaggtttggg ataatttaat
1201 ttcaagcaat taactcccat atatggccat gttacgtaac ttgtctaaca tcttaaaagc
1261 cggtgtttca gatactacac actctattgt gatcaacaag atttgtgagc ccaaggccgt
1321 tgagaactcc aagatgttcc ctcttcaatt ctttagtgcc attgaagctg ttaatgaagc
1381 agttactaag ggattcaagg ccaagaagag agaaaatatg aatcttaaag gtcaaatcga
1441 agcagtaaag gaagttgttg aaaaaaccga tgaagagaag aaagatatgg agttggagta
1501 aaccgaagaa ggagaatttg ttaaagtcaa cgaaggaatt ggcaagcaat acattaactc
1561 cattgaactt gcaatcaaga tagcagttaa caagaattta gatgaaatca aaggacacac
1621 tgcaatcttc tctgatgttt ctggttctat gagtacctca atgtcaggtg gagccaagaa
1681 gtatggttcc gttcgtactt gtctcgagtg tgcattagtc cttggtttga tggtaaaata
1741 acgttgtgaa aagtcctcat tctacatctt cagttcacct agttctcaat gcaataagtg
1801 ttacttagaa gttgatctcc ctggagacga actccgtcct tctatgtaaa aacttttgca
1861 agagaaagga aaacttggtg gtggtactga tttcccctat gagtgcattg atgaatggac
1921 aaagaataaa actcacgtag acaatatcgt tattttgtct gatatgatga ttgcagaagg
1981 atattcagat atcaatgtta gaggcagttc cattgttaac agcatcaaaa agtacaagga
2041 tgaagtaaat cctaacatta aaatctttgc agttgactta gaaggttacg gaaagtgcct
2101 taatctaggt gatgagttca atgaaaacaa ctacatcaag atattcggta tgagcgattc
2161 aatcttaaag ttcatttcag ccaagcaagg aggagcaaat atggtcgaag ttatcaaaaa
2221 ctttgccctt caaaaaatag gacaaaagtg agtttcttga gattcttcta taacaaaaat
2281 ctcaccccac ttttttgttt tattgcatag ccattatgaa atttaaatta ttatctattt
2341 atttaagtta cttacatagt ttatgtatcg cagtctatta gcctattcaa atgattctgc
2401 aaagaacaaa aaagattaaa a
```

FIGURE 20

MEIENNQAQQPKAEKLWWELELEMQENQNDIQVRVKIDDPKQYL

VNVTAACLLQEGSYYQDKDERRYIITKALLEVAESDPEFICQLAVYIRNELYIRTTTN

YIVAFCVVHKNTQPFIEKYFNKAVLLPNDLLEVCEFAQVLYIFDATEFKNLYLDRILS

QDIRKELTFRKCLQRCVRSKFSEFNEYQLGKYCTESQRKKTMFRYLSVTNKQKWDQTK

KKRKENLLTKLQAIKESEDKSKRETGDIMNVEDAIKALKPAVMKKIAKRQNAMKKHMK

APKIPNSTLESKYLTFKDLIKFCHISEPKERVYKILGKKYPKTEEEYKAAFGDSASAP

FNPELAGKRMKIEISKTWENELSAKGNTAEVWDNLISSNQLPYMAMLRNLSNILKAGV

SDTTHSIVINKICEPKAVENSKMFPLQFFSAIEAVNEAVTKGFKAKKRENMNLKGQIE

AVKEVVEKTDEEKKDMELEQTEEGEFVKVNEGIGKQYINSIELAIKIAVNKNLDEIKG

HTAIFSDVSGSMSTSMSGGAKKYGSVRTCLECALVLGLMVKQRCEKSSFYIFSSPSSQ

CNKCYLEVDLPGDELRPSMQKLLQEKGKLGGGTDFPYECIDEWTKNKTHVDNIVILSD

MMIAEGYSDINVRGSSIVNSIKKYKDEVNPNIKIFAVDLEGYGKCLNLGDEFNENNYI

KIFGMSDSILKFISAKQGGANMVEVIKNFALQKIGQK

FIGURE 21

1 tcaatactat taattaataa ataaaaaaaa gcaaactaca aagaaaatgt caaggcgtaa
61 ctaaaaaaag ccataggctc ctataggcaa tgaaacaaat cttgattttg tattacaaaa
121 tctagaagtt tacaaaagcc agattgagca ttataagacc tagtagtaat agatcaaaga
181 ggaggatctc aagcttttaa agttcaaaaa ttaagattag gatggaaact ctggcaacga
241 tgatgatgat gaagaaaaca actcaaataa ataataagaa ttattaagga gagtcaatta
301 gattaagtag caagtttaat tgataaaaaa agttggttct aaggtagaga aagatttgaa
361 tttgaacgaa gatgaaaaca aaaagaatgg actttctgaa tagcaagtga aagaagagta
421 attaagaacg attactgaag aataggttaa gtattaaaat ttagtattta acatggacta
481 ccagttagat ttaaatgaga gtggtggcca tagaagacac agaagagaaa cagattatga
541 tactgaaaaa tggtttgaaa tatctcatga ccaaaaaaat tatgtatcaa tttacgccaa
601 ctaaaagaca tcatattgtt ggtggcttaa agattatttt aataaaaaca attatgatca
661 tcttaatgta agcattaaca gactagaaac tgaagccgaa ttctatgcct ttgatgattt
721 ttcacaaaca atcaaactta ctaataattc ttactagact gttaacatag acgttaattt
781 tgataataat ctctgtatac tcgcattgct tagattttta ttatcactag aaagattcaa
841 tattttgaat ataagatctt cttatacaag aaattaatat aattttgaga aaattggtga
901 gctacttgaa actatcttcg cagttgtctt ttctcatcgc cacttacaag gcattcattt
961 acaagttcct tgcgaagcgt tctaatattt agttaactcc tcatcataaa ttagcgttaa
1021 agatagctaa ttataggtat actctttctc tacagactta aaattagttg acactaacaa
1081 agtccaagat tattttaagt tcttataaga attccctcgt ttgactcatg taagctagta
1141 ggctatccca gttagtgcta ctaacgctgt agagaacctc aatgttttac ttaaaaaggt
1201 caagcatgct aatcttaatt tagtttctat ccctacctaa ttcaattttg atttctactt
1261 tgttaattta taacatttga aattagagtt tggattagaa ccaaatattt tgacaaaaca
1321 aaagcttgaa aatctacttt tgagtataaa ataatcaaaa aatcttaaat ttttaagatt
1381 aaacttttac acctacgttg cttaagaaac ctccagaaaa cagatattaa aacaagctac
1441 aacaatcaaa aatctcaaaa acaataaaaa tcaagaagaa actcctgaaa ctaaagatga
1501 aactccaagc gaaagcacaa gtggtatgaa attttttgat catctttctg aattaaccga
1561 gcttgaagat ttcagcgtta acttgtaagc tacccaagaa atttatgata gcttgcacaa
1621 acttttgatt agatcaacaa atttaaagaa gttcaaatta agttacaaat atgaaatgga
1681 aaagagtaaa atggatacat tcatagatct taagaatatt tatgaaacct taaacaatct
1741 taaaagatgc tctgttaata tatcaaatcc tcatggaaac atttcttatg aactgacaaa
1801 taaagattct acttttata aatttaagct gaccttaaac taagaattat aacacgctaa
1861 gtatactttt aagtagaacg aattttaatt taataacgtt aaaagtgcaa aaattgaatc
1921 ttccttcatta gaaagcttag aagatattga tagtctttgc aaatctattg cttcttgtaa
1981 aaatttacaa aatgttaata ttatcgccag tttgctctat cccaacaata tttagaaaaa
2041 tcctttcaat aagcccaatc ttctattttt caagcaattt gaataattga aaaatttgga
2101 aaatgtatct atcaactgta ttcttgatca gcatatactt aattctattt cagaattctt
2161 agaaaagaat aaaaaaataa aagcattcat tttgaaaaga tattatttat tacaatatta
2221 tcttgattat actaaattat ttaaaacact tcaatagtta cctgaattaa attaagttta
2281 cattaattag caattagaag aattgactgt gagtgaagta cataagtaag tatgggaaaa
2341 ccacaagcaa aaagctttct atgaaccatt atgtgagttt atcaaagaat catcctaaac
2401 cctttagcta atagattttg accaaaacac tgtaagtgat gactctatta aaaagatttt
2461 agaatctata tctgagtcta agtatcatca ttatttgaga ttgaacccta gttaatctag
2521 cagtttaatt aaatctgaaa acgaagaaat ttaagaactt ctcaaagctt gcgacgaaaa
2581 aggtgtttta gtaaaagcat actataaatt ccctctatgt ttaccaactg gtacttatta
2641 cgattacaat tcagatagat ggtgattaat taaatattag tttaaataaa tattaaatat
2701 tgaatatttc tttgcttatt atttgaataa tacatacaat agtcattttt agtgttttga
2761 atatatttta gttatttaat tcattatttt aagtaaataa ttatttttca atcatttttt
2821 aaaaaatcg

FIGURE 22

MSRRNQKKPQAPIGNETNLDFVLQNLEVYKSQIEHYKTQQQQIK

EEDLKLLKFKNQDQDGNSGNDDDDEENNSNKQQELLRRVNQIKQQVQLIKKVGSKVEK

DLNLNEDENKKNGLSEQQVKEEQLRTITEEQVKYQNLVFNMDYQLDLNESGGHRRHRR

ETDYDTEKWFEISHDQKNYVSIYANQKTSYCWWLKDYFNKNNYDHLNVSINRLETEAE

FYAFDDFSQTIKLTNNSYQTVNIDVNFDNNLCILALLRFLLSLERFNILNIRSSYTRN

QYNFEKIGELLETIFAVVFSHRHLQGIHLQVPCEAFQYLVNSSSQISVKDSQLQVYSF

STDLKLVDTNKVQDYFKFLQEFPRLTHVSQQAIPVSATNAVENLNVLLKKVKHANLNL

VSIPTQFNFDFYFVNLQHLKLEFGLEPNILTKQKLENLLLSIKQSKNLKFLRLNFYTY

VAQETSRKQILKQATTIKNLKNNKNQEETPETKDETPSESTSGMKFFDHLSELTELED

FSVNLQATQEIYDSLHKLLIRSTNLKKFKLSYKYEMEKSKMDTFIDLKNIYETLNNLK

RCSVNISNPHGNISYELTNKDSTFYKFKLTLNQELQHAKYTFKQNEFQFNNVKSAKIE

SSSLESLEDIDSLCKSIASCKNLQNVNIIASLLYPNNIQKNPFNKPNLLFFKQFEQLK

NLENVSINCILDQHILNSISEFLEKNKKIKAFILKRYYLLQYYLDYTKLFKTLQQLPE

LNQVYINQQLEELTVSEVHKQVWENHKQKAFYEPLCEFIKESSQTLQLIDFDQNTVSD

DSIKKILESISESKYHHYLRLNPSQSSSLIKSENEEIQELLKACDEKGVLVKAYYKFP

LCLPTGTYYDYNSDRW

FIGURE 23

MKILFEFIQDKLDIDLQTNSTYKENLKCGHFNGLDEILTTCFAL

PNSRKIALPCLPGDLSHKAVIDHCIIYLLTGELYNNVLTFGYKIARNEDVNNSLFCHS

ANVNVTLLKGAAWKMFHSLVGTYAFVDLLINYTVIQFNGQFFTQIVGNRCNEPHLPPK

WVQRSSSSSATAAQIKQLTEPVTNKQFLHKLNINSSSFFPYSKILPSSSSIKKLTDLR

EAIFPTNLVKIPQRLKVRINLTLQKLLKRHKRLNYVSILNSICPPLEGTVLDLSHLSR

QSPKERVLKFIIVILQKLLPQEMFGSKKNKGKIIKNLNLLLSLPLNGYLPFDSLLKKL

RLKDFRWLFISDIWFTKHNFENLNQLAICFISWLFRQLIPKIIQTFFYCTEISSTVTI

VYFRHDTWNKLITPFIVEYFKTYLVENNVCRNHNSYTLSNFNHSKMRIIPKKSNNEFR

IIAIPCRGADEEEFTIYKENHKNAIQPTQKILEYLRNKRPTSFTKIYSPTQIADRIKE

FKQRLLKKFNNVLPELYFMKFDVKSCYDSIPRMECMRILKDALKNENGFFVRSQYFFN

TNTGVLKLFNVVNASRVPKPYELYIDNVRTVHLSNQDVINVVEMEIFKTALWVEDKCY

IREDGLFQGSSLSAPIVDLVYDDLLEFYSEFKASPSQDTLILKLADDFLIISTDQQQV

INIKKLAMGGFQKYNAKANRDKILAVSSQSDDDTVIQFCAMHIFVKELEVWKHSSTMN

NFHIRSKSSKGIFRSLIALFNTRISYKTIDTNLNSTNTVLMQIDHVVKNISECYKSAF

KDLSINVTQNMQFHSFLQRIIEMTVSGCPITKCDPLIEYEVRFTILNGFLESLSSNTS

KFKDNIILLRKEIQHLQAYIYIYIHIVN

FIGURE 24

Oxytricha LCVSYILSSFYYANLEENALQFLRKESMDPEKPETNLLMRLT
Euplotes LCVSSILSSFYYATLEESSLGFLRDESMNPENPNVNLLMRLT

FIGURE 25

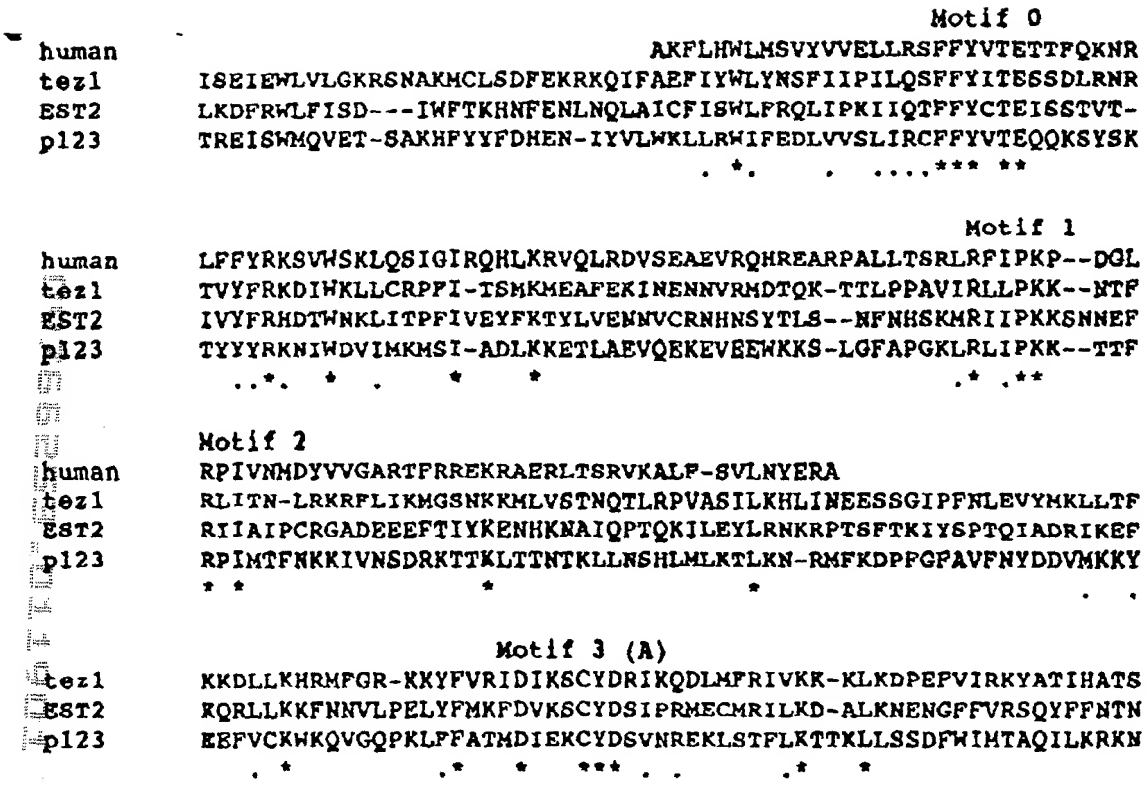
Motif 0
human AKFLHWLMSVYVVELLRSFFYVTETTFQKNR
tez1 ISEIEWLVLGKRSNAKMCLSDFEKRKQIFAEFIYWLYNSFIIPILQSFFYITESSDLRNR
EST2 LKDFRWLFISD---IWFTKHNFENLNQLAICFISWLFRQLIPKIIQTFFYCTEISSTVT-
p123 TREISWMQVET-SAKHFYYFDHEN-IYVLWKLLRWIFEDLVVSLIRCFFYVTEQQKSYSK
Motif 1
human LFFYRKSVWSKLQSIGIRQHLKRVQLRDVSEAEVRQHREARPALLTSRLRFIPKP--DGL
tez1 TVYFRKDIWKLLCRPPI-TSMKMEAFEKINENNVRMDTQK-TTLPPAVIRLLPKK--NTF
EST2 IVYFRHDTWNKLITPFIVEYFKTYLVENNVCRNHNSYTLS--NFNHSKMRIIPKKSNNEF
p123 TYYYRKNIWDVIMKMSI-ADLKKETLAEVQEKEVEEWKKS-LGFAPGKLRLIPKK--TTF
Motif 2
human RPIVNMDYVVGARTFRREKRAERLTSRVKALF-SVLNYERA
tez1 RLITN-LRKRFLIKMGSNKKMLVSTNQTLRPVASILKHLINEESSGIPFNLEVYMKLLTF
EST2 RIIAIPCRGADEEEFTIYKENHKNAIQPTQKILEYLRNKRPTSFTKIYSPTQIADRIKEF
p123 RPIMTFNKKIVNSDRKTTKLTTNTKLLNSHLMLKTLKN-RMFKDPFGFAVFNYDDVMKKY
Motif 3 (A)
tez1 KKDLLKHRMFGR-KKYFVRIDIKSCYDRIKQDLMFRIVKK-KLKDPEPVIRKYATIHATS
EST2 RQRLLKKFNNVLPELYFMKFDVKSCYDSIPRMECMRILKD-ALKNENGFFVRSQYFFNTN
p123 EEFVCKWKQVGQPKLFFATMDIEKCYDSVNREKLSTFLKTTKLLSSDFWIHTAQILKRKN

FIGURE 26

ATTTATACTCATGAAAATCTTATTCGAGTTCATTCAAGACAAGCTTGACATTGATCTACA
GACCAACAGTACTTACAAAGAAAATTTAAAATGTGGTCACTTCAATGGCCTCGATGAAAT
TCTAACTACGTGTTTCGCACTACCAAATTCAAGAAAAATAGCATTACCATGCCTTCCTGG
TGACTTAAGCCACAAAGCAGTCATTGATCACTGCATCATTTACCTGTTGACGGGCGAATT
ATACAACAACGTACTAACATTTGGCTATAAAATAGCTAGAAATGAAGATGTCAACAATAG
TCTTTTTTGCCATTCTGCAAATGTTAACGTTACGTTACTGAAAGGCGCTGCTTGGAAAAT
GTTCCACAGTTTGGTCGGTACATACGCATTCGTTGATTTATTGATCAATTATACAGTAAT
TCAATTTAATGGGCAGTTTTTCACTCAAATCGTGGGTAACAGATGTAACGAACCTCATCT
GCCGCCCAAATGGGTCCAACGATCATCCTCATCATCCGCAACTGCTGCGCAAATCAAACA
ACTTACAGAACCAGTGACAAATAAACAATTCTTACACAAGCTCAATATAAATTCCTCTTC
TTTTTTTCCTTATAGCAAGATCCTTCCTTCATCATCATCTATCAAAAAGCTAACTGACTT
GAGAGAAGCTATTTTTCCCACAAATTTGGTTAAAATTCCTCAGAGACTAAAGGTACGAAT
TAATTTGACGCTGCAAAAGCTATTAAAGAGACATAAGCGTTTGAATTACGTTTCTATTTT
GAATAGTATTTGCCCACCATTGGAAGGGACCGTATTGGACTTGTCGCATTTGAGTAGGCA
ATCACCAAAGGAACGAGTCTTGAAATTTATCATTGTTATTTTACAGAAGTTATTACCCCA
AGAAATGTTTGGCTCAAAGAAAAATAAAGGAAAAATTATCAAGAATCTAAATCTTTTATT
AAGTTTACCCTTAAATGGCTATTTACCATTTGATAGTTTGTTGAAAAAGTTAAGATTAAA
GGATTTTCGGTGGTTGTTCATTTCTGATATTTGGTTCACCAAGCACAATTTTGAAAACTT
GAATCAATTGGCGATTTGTTTCATTTCCTGGCTATTTAGACAACTAATTCCCAAAATTAT
ACAGACTTTTTTTTACTGCACCGAAATATCTTCTACAGTGACAATTGTTTACTTTAGACA
TGATACTTGGAATAAACTTATCACCCCTTTTATCGTAGAATATTTTAAGACGTACTTAGT
CGAAAACAACGTATGTAGAAACCATAATAGTTACACGTTGTCCAATTTCAATCATAGCAA
AATGAGGATTATACCAAAAAAAAGTAATAATGAGTTCAGGATTATTGCCATCCCATGCAG
AGGGGCAGACGAAGAAGAATTCACAATTTATAAGGAGAATCACAAAAATGCTATCCAGCC
CACTCAAAAAATTTTAGAATACCTAAGAAACAAAAGGCCGACTAGTTTTACTAAAATATA
TTCTCCAACGCAAATAGCTGACCGTATCAAAGAATTTAAGCAGAGACTTTTAAAGAAATT
TAATAATGTCTTACCAGAGCTTTATTTCATGAAATTTGATGTCAAATCTTGCTATGATTC
CATACCAAGGATGGAATGTATGAGGATACTCAAGGATGCGCTAAAAAATGAAAATGGGTT
TTTCGTTAGATCTCAATATTTCTTCAATACCAATACAGGTGTATTGAAGTTATTTAATGT
TGTTAACGCTAGCAGAGTACCAAAACCTTATGAGCTATACATAGATAATGTGAGGACGGT
TCATTTATCAAATCAGGATGTTATAAACGTTGTAGAGATGGAAATATTTAAAACAGCTTT
GTGGGTTGAAGATAAGTGCTACATTAGAGAAGATGGTCTTTTTCAGGGCTCTAGTTTATC
TGCTCCGATCGTTGATTTGGTGTATGACGATCTTCTGGAGTTTTATAGCGAGTTTAAAGC
CAGTCCTAGCCAGGACACATTAATTTTAAAACTGGCTGACGATTTCCTTATAATATCAAC
AGACCAACAGCAAGTGATCAATATCAAAAAGCTTGCCATGGGCGGATTTCAAAAATATAA
TGCGAAAGCCAATAGAGACAAAATTTTAGCCGTAAGCTCCCAATCAGATGATGATACGGT
TATTCAATTTTGTGCAATGCACATATTTGTTAAAGAATTGGAAGTTTGGAAACATTCAAG
CACAATGAATAATTTCCATATCCGTTCGAAATCTAGTAAAGGGATATTTCGAAGTTTAAT
AGCGCTGTTTAACACTAGAATCTCTTATAAAACAATTGACACAAATTTAAATTCAACAAA
CACCGTTCTCATGCAAATTGATCATGTTGTAAAGAACATTTCGGAATGTTATAAATCTGC
TTTTAAGGATCTATCAATTAATGTTACGCAAAATATGCAATTTCATTCGTTCTTACAACG
CATCATTGAAATGACAGTCAGCGGTTGTCCAATTACGAAATGTGATCCTTTAATCGAGTA
TGAGGTACGATTCACCATATTGAATGGATTTTTGGAAAGCCTATCTTCAAACACATCAAA
ATTTAAAGATAATATCATTCTTTTGAGAAAGGAAATTCAACACTTGCAAGC

FIGURE 27

AKFLHWLMSVYYVELLRSFFYVTETTFQKNRLFFYRKSVWSKLQSIGIRQHLKR
VQLRDVSEAEVRQHREARPALLTSRLRFIPKPDGLRPIVNMDYVVGARTFRREKR
AERLTSRVKALFSVLNYERA

FIGURE 28

GCCAAGTTCCTGCACTGGCTGATGAGTGTGTACGTCGTCGAGCTGCTCAGGTC
TTTCTTTTATGTCACGGAGACCACGTTTCAAAAGAACAGGCTCTTTTTCTACC
GGAAGAGTGTCTGGAGCAAGTTGCAAAGCATTGGAATCAGACAGCACTTGAA
GAGGGTGCAGCTGCGGGACGTGTCGGAAGCAGAGGTCAGGCAGCATCGGGA
AGCCAGGCCCGCCCTGCTGACGTCCAGACTCCGCTTCATCCCCAAGCCTGACG
GGCTGCGGCCGATTGTGAACATGGACTACGTCGTGGGAGCCAGAACGTTCCG
CAGAGAAAAGAGGGCCGAGCGTCTCACCTCGAGGGTGAAGGCACTGTTCAGC
GTGCTCAACTACGAGCGGGCGCG

FIGURE 29

MTEHHTPKSRILRFLENQYVYLCTLNDYVQLVLRGSPASSYSNICERLRSDVQTSFSIFLHSTVVGF
DSKPDEGVQFSSPKCSQSELIANVVKQMFDESFERRRNLLMKGFSMNHEDFRAMHVNGVQNDLV
STFPNYLISILESKNWQLLLEIIGSDAMHYLLSKGSIFEALPNDNYLQISGIPLFKNNVFEETVSKKRK
RTIETSITQNKSARKEVSWNSISISRFSIFYRSSYKKFKQDLYFNLHSICDRNTVHMWLQWIFPRQFG
LINAFQVKQLHKVIPLVSQSTVVPKRLLKVYPLIEQTAKRLHRISLSKVYNHYCPYIDTHDDEKILS
YSLKPNQVFAFLRSILVRVFPKLIWGNQRIFEIILKDLETFLKLSRYESFSLHYLMSNIKISEIEWLVL
GKRSNAKMCLSDFEKRKQIFAEFIYWLYNSFIIPILQSFFYITESSDLRNRTVYFRKDIWKLLCRPFIT
SMKMEAFEKINENNVRMDTQKTTLPPAVIRLLPKKNTFRLITNLRKRFLIKMGSNKKMLVSTNQT
LRPVASILKHLINEESSGIPFNLEVYMKLLTFKKDLLKHRMFGRKKYFVRIDIKSCYDRIKQDLMFR
IVKKKLKDPEFVIRKYATIHATSDRATKNFVSEAFSYFDMVPFEKVVQLLSMKTSDTLFVDFVDY
WTKSSSEIFKMLKEHLSGHIVKIGNSQYLQKVGIPQGSILSSFLCHFYMEDLIDEYLSFTKKKGSVL
LRVVDDFLFITVNKKDAKKFLNLSLRGFEKHNFSTSLEKTVINFENSNGIINNTFFNESKKRMPFFG
FSVNMRSLDTLLACPKIDEALFNSTSVELTKHMGKSFFYKILRSSLASFAQVFIDITHNSKFNSCCNI
YRLGYSMCMRAQAYLKRMKDIFIPQRMFITDLLNVIGRKIWKKLAEILGYTSRRFLSSAEVKWLFC
LGMRDGLKPSFKYHPCFEQLIYQFQSLTDLIKPLRPVLRQVLFLHRRIAD

FIGURE 30

ggtaccgatttactttcctttcttcataagctaattgcttcctcgaacgctcctaaatctctggaaatatttttacaagaactcaataacaataccaagtcaaattccaatatgaagg
tgttattagtgatcgataatatttctattttatcggtcgttaccaagtataaggacaaaaagaacaacttccttcccccctaaagacttttactttattaatttacttttcaaatatatttcg
ggttcgcttacttttaatcgtggtactgttttagctgctacttctagccaaccgcgtgtttctaccccgtcattggatatagctcttggagtagctcacagaaatccttacaaatctt
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aaaaggttgataattatttgcaaaatcatgtccttagtggtggtaatccgcgaaagtttttttgatgcttgcacacgtctagcatgattgagatattcaaaaatttctatccactacaa
ctcctttaacgcggttttattttctattttctattctcatgttgttccaaatatgtatcatctcgtattaggctttttttccgtttttactcctggaatcgtaccttttttcactattccccctaatg
aataatctaaattagtttcgcttataattgatagtagtagaaagattggtgattctactcgtgtaatgttattagtttaaagatactttgcaaaacatttattagctatcattatataaaa
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GACCGAACACCATACCCCCAAAAGCAGGATTCTTCGCTTTCTAGAGAATCAATATGTATACCTATGTA
CCTTAAATGATTATGTACAACTTGTTTTGAGAGGGTCGCCGGCAAGCTCGTATAGCAATATATGCGAA
CGCTTGAGAAGCGATGTACAAACGTCCTTTTCTATTTTTCTTCATTCGACTGTAGTCGGCTTCGACAGT
AAGCCAGATGAAGGTGTTCAATTTTCTTCTCCAAAATGCTCACAGTCAGAGgtatatatatttttgttttgattttttctattcg
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ATCTACTGATGAAAGGGTTTTCCATGgtaaggtattctaattgtgaaatatttacctgcaattactgtttcaaagagattgtatttaaccgataaagAA
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CAAATGACAATTACCTTCAGATTTCTGGCATACCACTTTTTAAAAATAATGTGTTTGAGGAAACTGTGT
CAAAAAAAAGAAAGCGAACCATTGAAACATCCATTACTCAAAATAAAAGCGCCCGCAAAGAAGTTTC
CTGGAATAGCATTTCAATTAGTAGGTTTAGCATTTTTTACAGGTCATCCTATAAGAAGTTTAAGCAAGgt
aactaatactgttatccttcataactaattttagATCTATATTTTAACTTACACTCTATTTGTGATCGGAACACAGTACACATG
TGGCTTCAATGGATTTTTCCAAGGCAATTTGGACTTATAAACGCATTTCAAGTGAAGCAATTGCACAA
AGTGATTCCACTGGTATCACAGAGTACAGTTGTGCCCAAACGTCTCCTAAAGGTATACCCTTTAATTGA
ACAAACAGCAAAGCGACTCCATCGTATTTCTCTATCAAAAGTTTACAACCATTATTGCCCATATATTGA
CACCCACGATGATGAAAAAATCCTTAGTTATTCCTTAAAGCCGAACCAGGTGTTTGCGTTTCTTCGATC
CATTCTTGTTCGAGTGTTTCCTAAATTAATCTGGGGTAACCAAAGGATATTTGAGATAATATTAAAAGg
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ATTATTTAATGAGTAACATAAAGgtaatatgccaaattttttttaccattaattaacaatcagATTTCAGAAATTGAATGGCTAGT
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TGTTAGGATGGATACTCAGAAAACTACTTTGCCTCCAGCAGTTATTCGTCTATTACCTAAGAAGAATAC
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AAACATTTAATCAATGAAGAAAGTAGTGGTATTCCATTTAACTTGGAGGTTTACATGAAGCTTCTTACT
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AAAAAGAAACTCAAGGATCCCGAATTTGTAATTCGAAAGTATGCAACCATACATGCAACAAGTGACCG
AGCTACAAAAAACTTTGTTAGTGAGGCGTTTTCCTATTgtaagtttatttttttcattggaatttttttaacaaattctttttttagTTGATAT
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ATACATTGTTAGCATGTCCTAAAATTGATGAAGCCTTATTTAACTCTACATCTGTAGAGCTGACGAAAC
ATATGGGGAAATCTTTTTTTTACAAAATTCTAAGgtatactgtgtaactgaataatagctgacaaataatcagATCGAGCCTTGC
ATCCTTTGCACAAGTATTTATTGACATTACCCACAATTCAAAATTCAATTCTTGCTGCAATATATATATAG
GCTAGGATACTCTATGTGTATGAGAGCACAAGCATACTTAAAAAGGATGAAGGATATATTTATTCCCC
AAAGAATGTTCATAACGGgtgagtacttattttaactagaaaagtcattaattaaccttagATCTTTTGAATGTTATTGGAAGAAAA
ATTTGGAAAAAGTTGGCCGAAATATTAGGATATACGAGTAGGCGTTTCTTGTCCTCTGCAGAAGTCAA

FIGURE 30 (cont.)

ATGgtacgtgtcggtctcgagacttcagcaatattgacacatcagGCTTTTTTGTCTTGGAATGAGAGATGGTTTGAAACCCTCTT
TCAAATATCATCCATGCTTCGAACAGCTAATATACCAATTTCAGTCATTGACTGATCTTATCAAGCCGC
TAAGACCAGTTTTGCGACAGGTGTTATTTTTACATAGAAGAATAGCTGATTAAtgtcattttcaatttattatatacatcctt
tattactggtgtcttaaacaatattattactaagtatagctgacccccaaagcaagcatactataggatttctagtaaagtaaaattaatctcgttattagttttgattgacttgtcttt
atccttatacttttaagaaagattgacagtggttgctgactactgcccacatgcccattaaacgggagtggttaaacattaaaagtaatacatgaggctaatctcctttcatttag
aataaggaaagtggttttctataatgaataatgcccgcactaatgcaaaaagacgaagattatcttctaaacaaggggggattaagcatatccgaaggaaaagagagtaatat
acccagtgttgttgaagaaagcaaggataatttggaacaagcttctgcagatgacaggctaaattttggtgaccgaattttggtaaaagccccaggttatccatggtggccg
gccttgctactgagacgaaaagaaactaaggatagtttgaatactaatagctcatttaatgtcttatataaggttttgtttttcctgacttcaattttgcatgggtgaaaagaaata
gtgttaagccattattggattccgaaatagccaaatttcttggttcctcaaagcggaagtctaaagaacttattgaagcttatgaggcttcaaaaactcctcctgatttaaaggag
gaatcttccaccgatgaggaaatggatagcttatcagctgctgaggagaagcctaatttttttgcaaaaaagaaaatatcattgggagacatctcttgatgaatcagatgcgga
gagtatctccagcggatccttgatgtcaataacttctatttctgaaatgtatggtcctactgtcgcttcgacttctcgtagctctacgcagttaagtgaccaaaggtacc

FIGURE 31

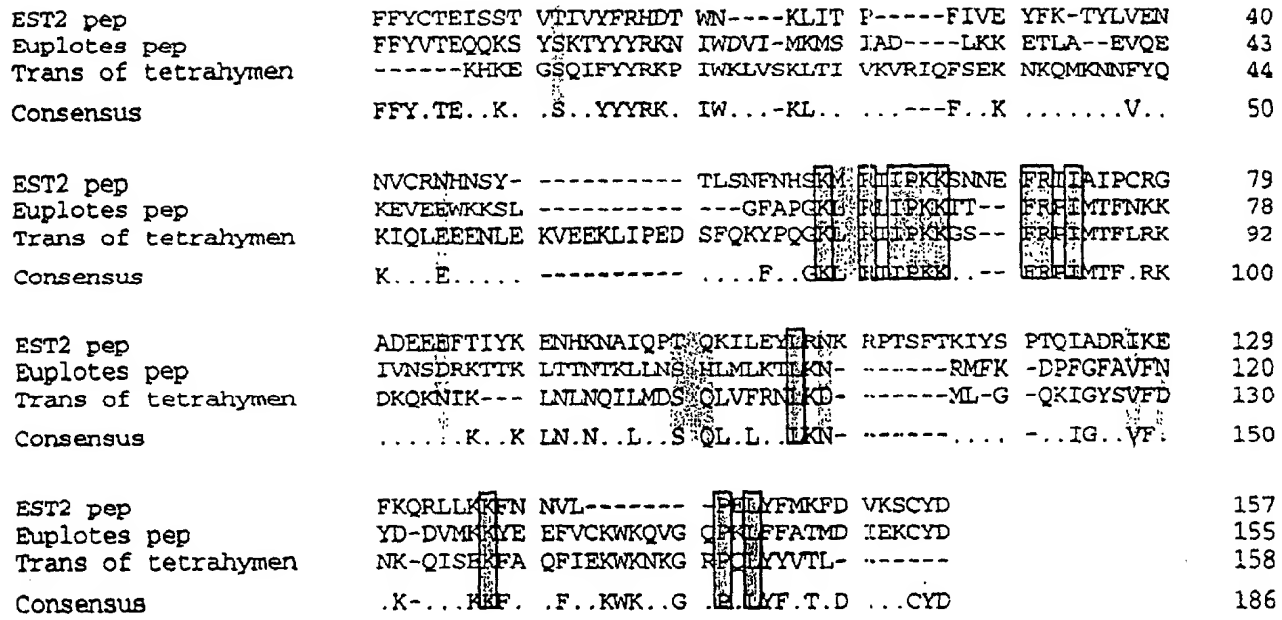

EST2 pep FFYCTEISST VTIVYFRHDT WN----KLIT P-----FIVE YFK-TYLVEN 40
Euplotes pep FFYVTEQQKS YSKTYYYRKN IWDVI-MKMS IAD----LKK ETLA--EVQE 43
Trans of tetrahymen ------KHKE GSQIFYYRKP IWKLVSKLTI VKVRIQFSEK NKQMKNNFYQ 44
Consensus FFY.TE..K. .S..YYYRK. IW...-KL.. ...---F..K .....V.. 50
EST2 pep NVCRNHNSY- ---------- TLSNFNHSKM FLIPKKSNNE FRIIAIPCRG 79
Euplotes pep KEVEEWKKSL ---------- ---GFAPCKL FLIPKKITT- FRKIMTFNKK 78
Trans of tetrahymen KIQLEEENLE KVEEKLIPED SFQKYPQCKL FLIPKKGS-- FRHIMTFLRK 92
Consensus K...E..... ---------- ....F..CKL FLIPKK..-- FRHIMTF.RK 100
EST2 pep ADEEEFTIYK ENHKNAIQPT QKILEYIRNK RPTSFTKIYS PTQIADRIKE 129
Euplotes pep IVNSDRKTTK LTTNTKLLNS HLMLKTIKN- -------RMFK -DPFGFAVFN 120
Trans of tetrahymen DKQKNIK--- LNLNQILMDS QLVFRNIKD- -------ML-G -QKIGYSVFD 130
Consensus .....K..K LN.N..L..S QL.L..IKN- ---------... -..IG..VF. 150
EST2 pep FKQRLLKKFN NVL------- -PHLYFMKFD VKSCYD 157
Euplotes pep YD-DVMKKYE EFVCKWKQVG QFKLFFATMD IEKCYD 155
Trans of tetrahymen NK-QISKKFA QFIEKWKNKG RPQLYYVTL- ------ 158
Consensus .K-...KKF. .F..KWK..G .P.LYF.T.D ...CYD 186

FIGURE 32

S-1: FFY VTE TTF QKN RLF FYR KSV WSK
S-2: RQH LKR VQL RDV SEA EVR QHR EA
S-3: AFT FRR EKR AER LTS RVK ALF SVL NYE

A-1: AKF LHW LMS VYV VEL LRS FFY VTE TTF Q
A-2: LFF YRK SVW SKL QSI GIR QHL KRV QLR DVS
A-3: PAL LTS RLR FIP KPD GLR PIV NMD YVV

FIGURE 33

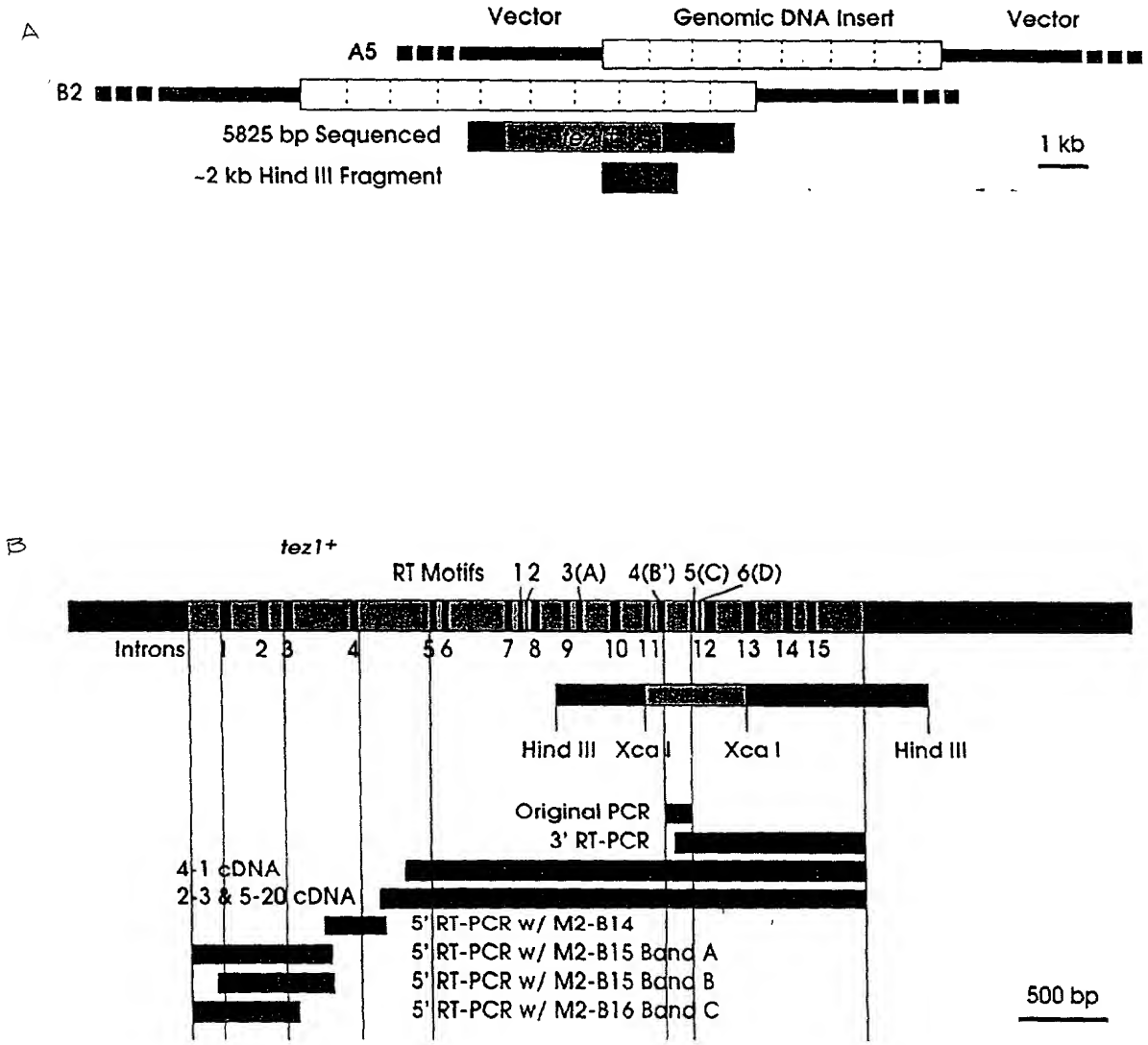

A
Vector
Genomic DNA Insert
Vector
A5
B2
5825 bp Sequenced
tez1+
1 kb
~2 kb Hind III Fragment
B
tez1+
RT Motifs 1 2 3(A) 4(B') 5(C) 6(D)
Introns 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Hind III
Xca I
Xca I
Hind III
Original PCR
3' RT-PCR
4-1 cDNA
2-3 & 5-20 cDNA
5' RT-PCR w/ M2-B14
5' RT-PCR w/ M2-B15 Band A
5' RT-PCR w/ M2-B15 Band B
5' RT-PCR w/ M2-B16 Band C
500 bp

FIGURE 34

Poly 4

```
          t       t       c
    t a   a   g   c   c   t c g
5'- cag acc aaa gga att cca taa gg -3'
    Q   T   K   G   I   P   Q   G
```

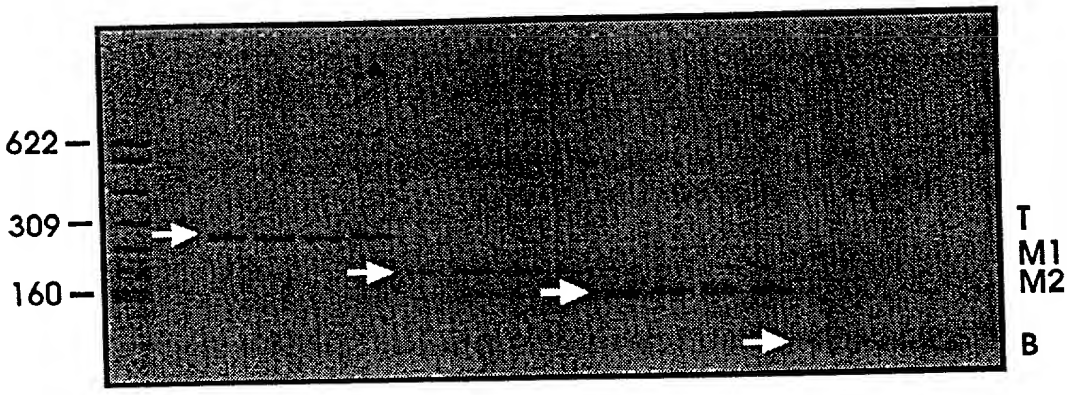
4 (B')

5 (c')

```
    D   D   Y   L   L   I   T
3'- ctg ctg atg gag gag tag tgg -5'
      a   a   a a a a a   a   a
                t   t   t   t
                        c   c
```

Poly 1

FIGURE 35



Motif B' (4)

QTKGIPQG

Motif C (5)

DDYLLIT

FIGURE 36

PCR Product M2 showed Reasonable Match with Other Telomerase Proteins

```
Ot                  LCVSYILSSFYYANLEENALQFLRKESMDPEKPETNLLMRLT
Ea_p123       KGIPQGLCVSSILSSFYYATLEESSLGFLRDESMNPENPNVNLLMRLTDDYLLIT
Sp_M2               SILSSFLCHFYMEDLIDEYLSFTKKK--------GSVLLRVV
Sc_p103       DGLFQGSSLSAPIVDLVYDDLLEFYSEFKASPS------QDTLILKLADDFLIIS
                         .*   .        * .    *              .....
```

```
Q   K   V   G   I   P   Q   G
Caa aaa gtt ggt atc cct cag gg......    <---Actual Genomic Sequence.

Poly 4
      t       t       c
t a   a   g   c   c   t c g
cag acc aaa gga att cca taa gg ---->

ag acc aaa gga att cca tca ggC TCA ATT CTG TCA TCT TTT TTG TGT CAT TTC TAT ATG
tc tgg ttt cct taa ggt agt ccG AGT TAA GAC AGT AGA AAA AAC ACA GTA AAG ATA TAC

        K   G   I   P   S   G   S   I   L   S   S   F   L   C   H   F   Y   M


GAA GAT TTG ATT GAT GAA TAC CTA TCG TTT ACG AAA AAG AAA GGA TCA GTG TTG TTA CGA
CTT CTA AAC TAA CTA CTT ATG GAT AGC AAA TGC TTT TTC TTT CCT AGT CAC AAC AAT GCT

E   D   L   I   D   E   Y   L   S   F   T   K   K   K   G   S   V   L   L   R


GTA GTC gac gac tac ctc ctc atc acc
CAT CAG ctg ctg atg gag gag tag tgg

V   V   D   D   Y   L   L   I   T

  <---- ctg ctg atg gag gag tag tgg
          a   a   a a a a a   a   a
                      t   t   t   t
                      c   c
                            Poly 1

   .....gac gat ttc ctc ttt ata aca......  <---Actual Genomic Sequence.
        D   D   F   L   F   I   T
```

FIGURE 37

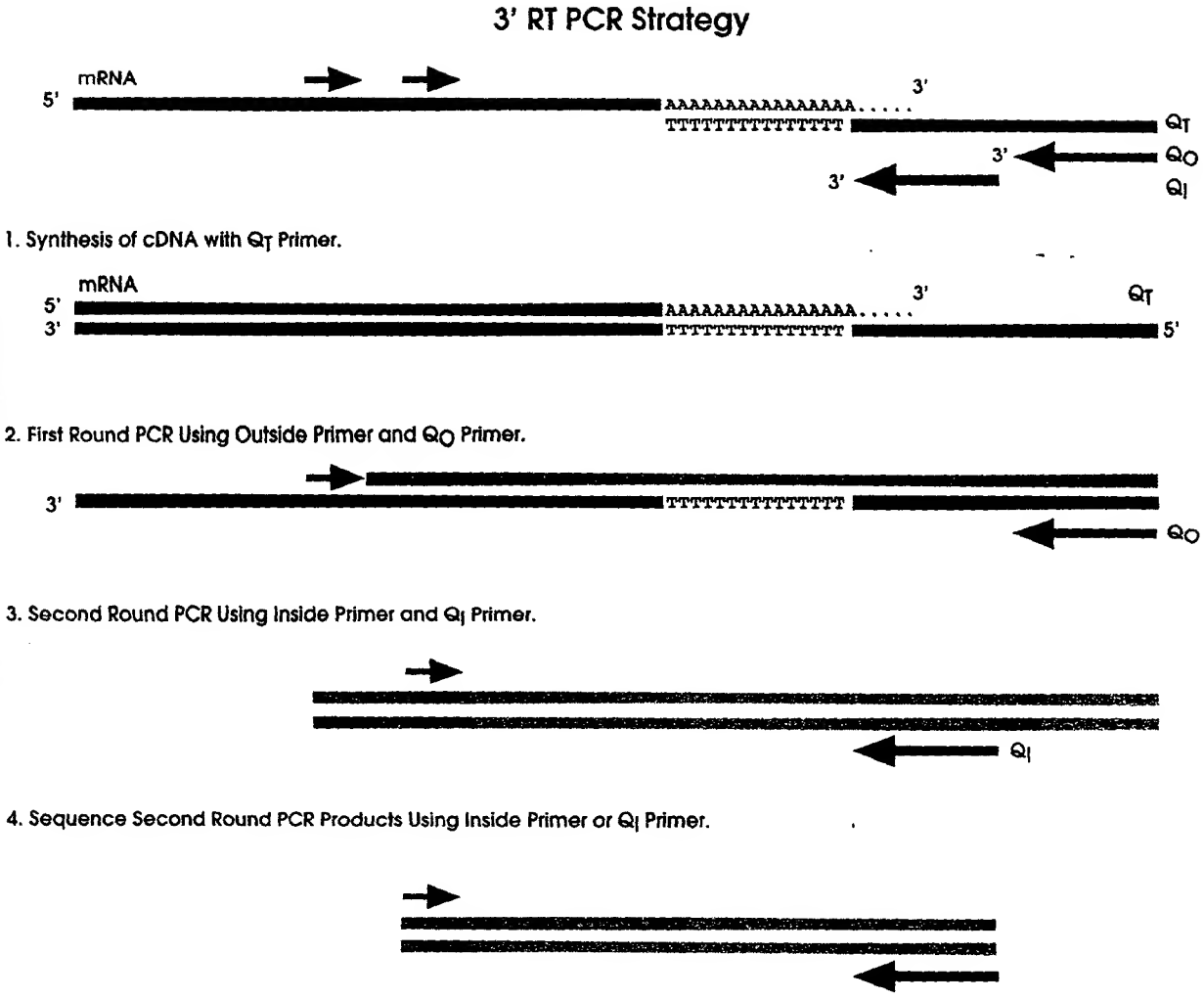

3' RT PCR Strategy
mRNA
5'
3'
AAAAAAAAAAAAAAAA.....
TTTTTTTTTTTTTTTT
Q_T
3'
Q_O
3'
Q_I
1. Synthesis of cDNA with Q_T Primer.
mRNA
5'
3'
3'
AAAAAAAAAAAAAAAA.....
TTTTTTTTTTTTTTTT
Q_T
5'
2. First Round PCR Using Outside Primer and Q_O Primer.
3'
TTTTTTTTTTTTTTTT
Q_O
3. Second Round PCR Using Inside Primer and Q_I Primer.
Q_I
4. Sequence Second Round PCR Products Using Inside Primer or Q_I Primer.

FIGURE 38

A

-Size Selected Libraries from P. Nurese

- 3 ~ 4 kb
- 5 ~ 6 kb
- 7 ~ 8 kb
- 11 ~ 12 kb

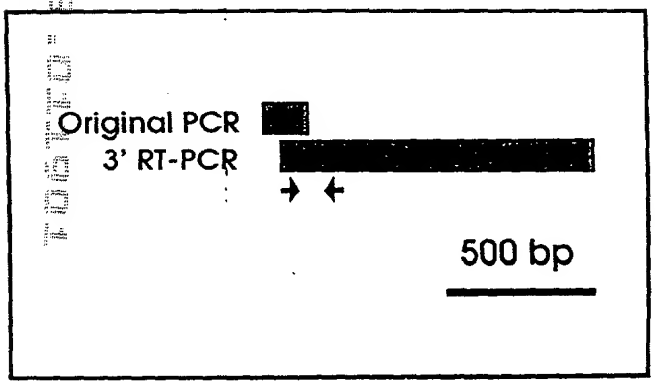
-Libraries from J.A. Wise

- Sau 3a Partial Digest
- Hind III Partial Digest

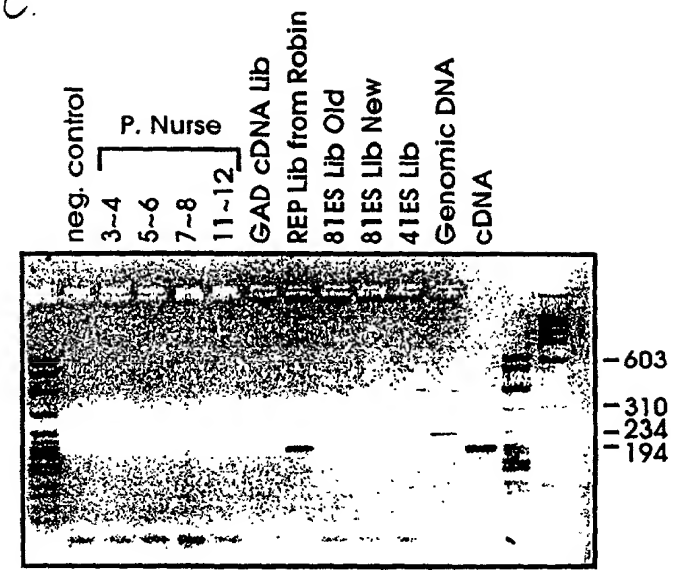
cDNA Libraries

- GAD (Gal Activation Domain) Library
- REP Library from R. Allshire
- REP81ES Library (old)
- REP81ES Library (new)
- REP41ES Library

B.



C.



D.

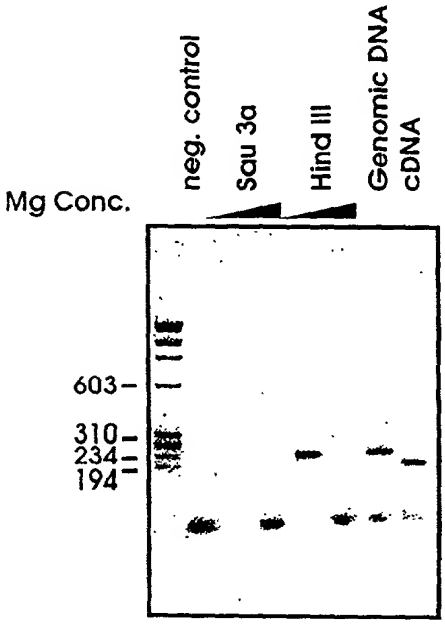
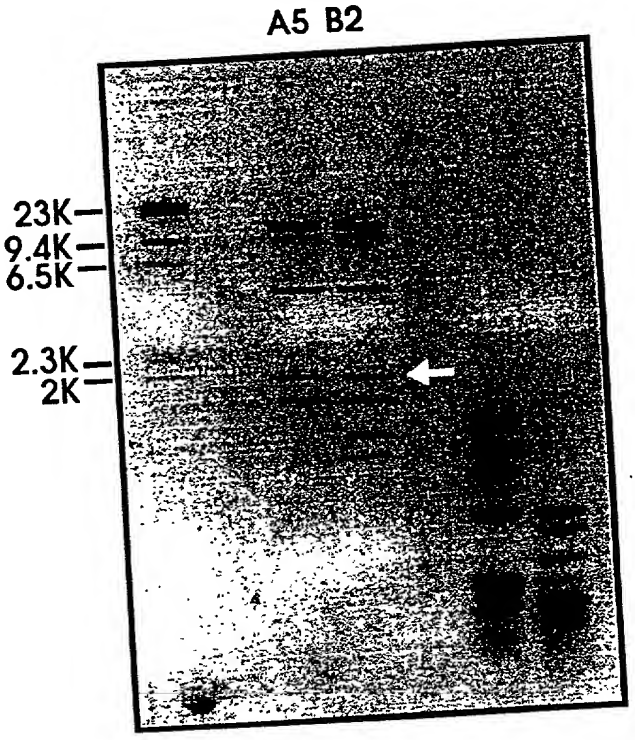


FIGURE 39



Hind III Digested Positive Genomic Clones

FIGURE 40

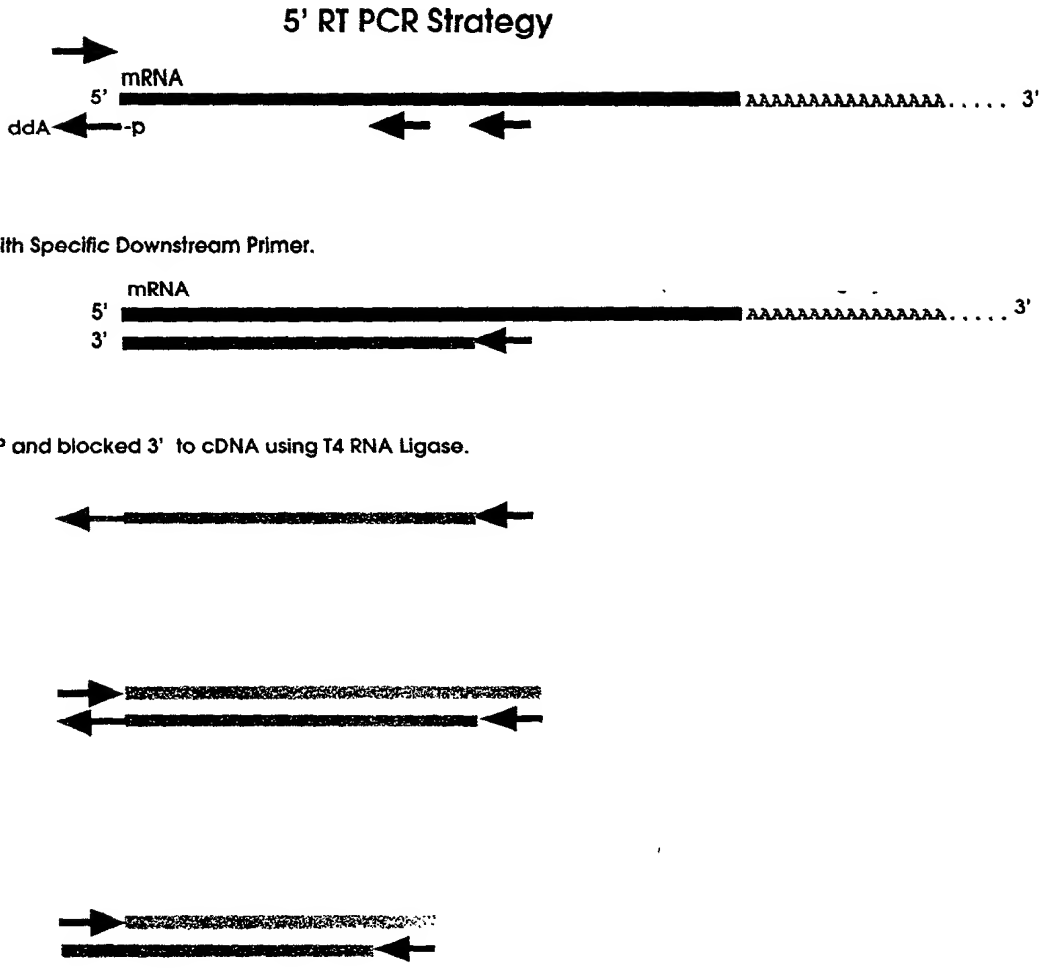

5' RT PCR Strategy
mRNA
5'
AAAAAAAAAAAAAAAA..... 3'
ddA
-p
1. Synthesis of cDNA with Specific Downstream Primer.
mRNA
5'
AAAAAAAAAAAAAAAA..... 3'
3'
2. Ligate Oligo with 5'-P and blocked 3' to cDNA using T4 RNA Ligase.
3. First Round PCR
4. Second Round PCR

FIGURE 41

Alignment of RT Domains from Telomerase Catalytic Subunits.

```
                                  Motif O
S.p. Tez1p (429). WLYNSFIIPILQSFFYITESSDLRNRTVYFRKDIW ...(35)...
S.c. Est2p (366). WLFRQLIPKIIQTFFYCTEISSTVT-IVYFRHDTW ...(35)...
E.a. p123  (441). WIFEDLVVSLIRCFFYVTEQQKSYSKTYYYRKNIW ...(35)...
                   *             *** **          * *   *

                    Motif 1    Motif 2     K
                   p hh h K     hR h       R
S.p. Tez1p  AVIRLLPKK--NTFRLITN-LRKRF ...(61)...
S.c. Est2p  SKMRIIPKKSNNEFRIIAIPCRGAD ...(62)...
E.a. p123   GKLRLIPKK--TTFRPIMTFNKKIV ...(61)...
              *  ***    ** *
                   Motif 3(A) AF
                      h  hDh  GY  h
S.p. Tez1p  KKYFVRIDIKSCYDRIKQDLMFRIVK ...(89)...
S.c. Est2p  ELYFMKFDVKSCYDSIPRMECMRILK ...(75)...
E.a. p123   KLFFATMDIEKCYDSVNREKLSTFLK ...(107)...
              *   *   ***            *
                    Motif 4(B')
                         hPQG   pP hh   h
S.p. Tez1p  YLQKVGIPQGSILSSFLCHFYMEDLIDEYLSF ...(6)...
S.c. Est2p  YIREDGLFQGSSLSAPIVDLVYDDLLEFYSEF ...(8)...
E.a. p123   YKQTKGIPQGLCVSSILSSFYYATLEESSLGF ...(14)...
            *    *  **   *           *      *
                    Y Motif 5(C)                    Motif 6(D)
                    h  F DDhhh                      Gh h  cK  h
S.p. Tez1p  VLLRVVDDFLFITVNKKDAKKFLNLSLRGFEKHNFSTSLEKTVINFENS .(205)
S.c. Est2p  LILKLADDFLIISTDQQQVINIKKLAMGGFQKYNAKANRDKILAVSSQS .(173)
E.a. p123   LLMRLTDDYLLITTQENNAVLFIEKLINVSRENGFKFNMKKLQTSFPLS .(209)
                  ** * *                                 *       *
```

FIGURE 42

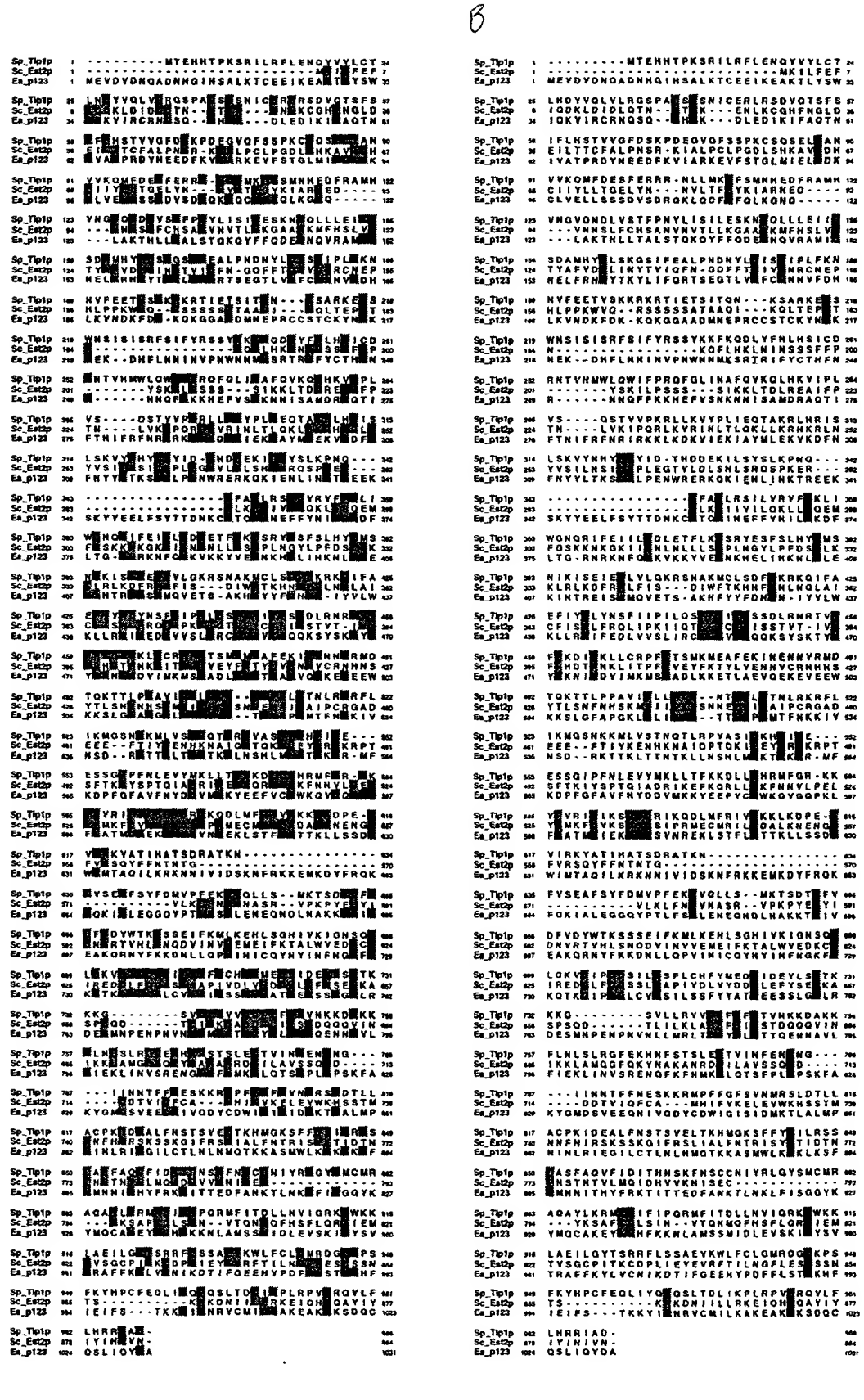
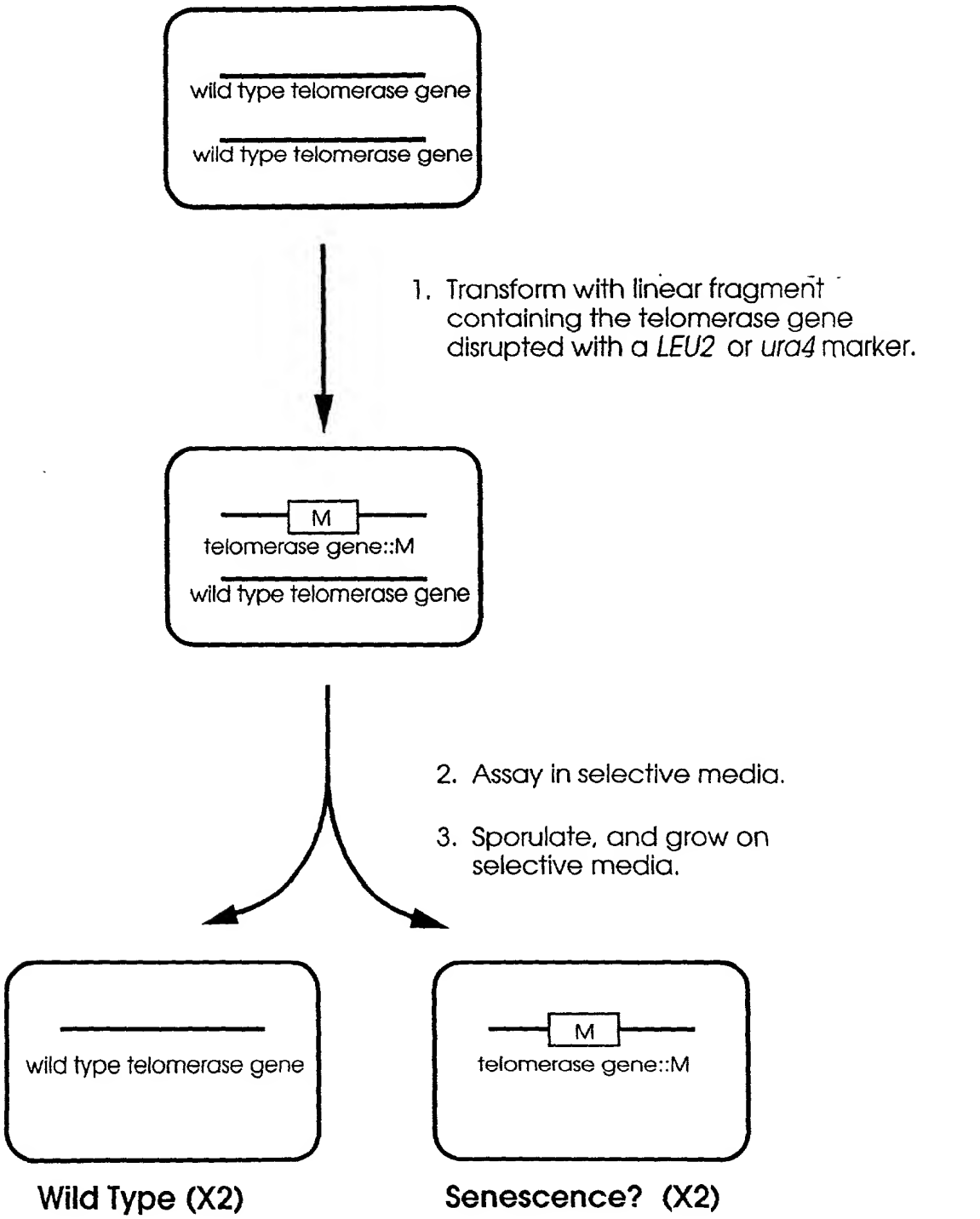


FIGURE 43

Disruption strategy for the putative telomerase genes.



(These cells will show a senescence phenotype if the disrupted gene encodes a telomerase subunit.)

FIGURE 44

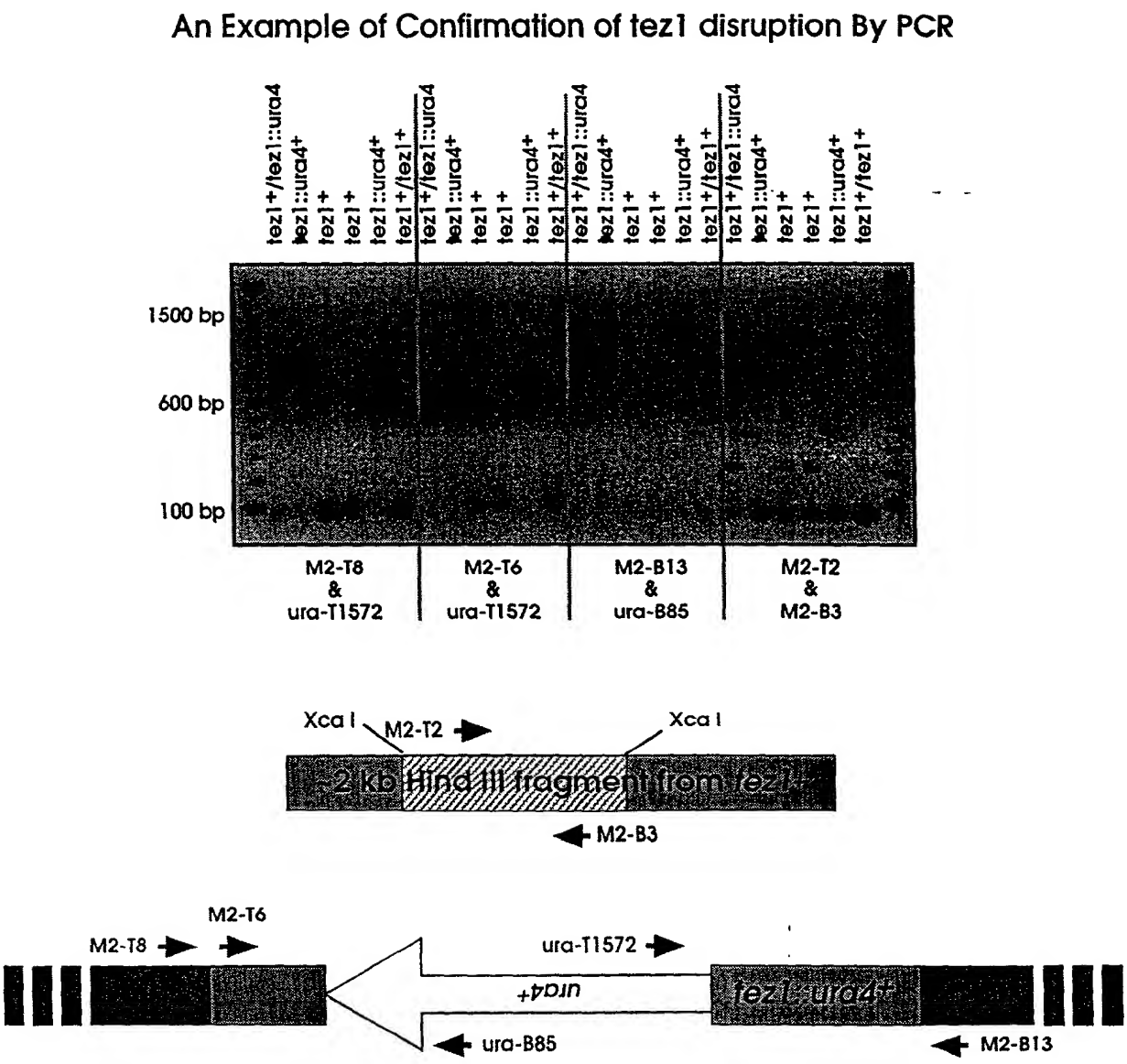

An Example of Confirmation of tez1 disruption By PCR
tez1+/tez1::ura4
tez1::ura4+
tez1+
tez1+
tez1::ura4+
tez1+/tez1+
1500 bp
600 bp
100 bp
M2-T8 & ura-T1572
M2-T6 & ura-T1572
M2-B13 & ura-B85
M2-T2 & M2-B3
Xca I
M2-T2
Xca I
~2 kb Hind III fragment from tez1+
M2-B3
M2-T6
M2-T8
ura-T1572
ura4+
tez1::ura4+
ura-B85
M2-B13

FIGURE 45

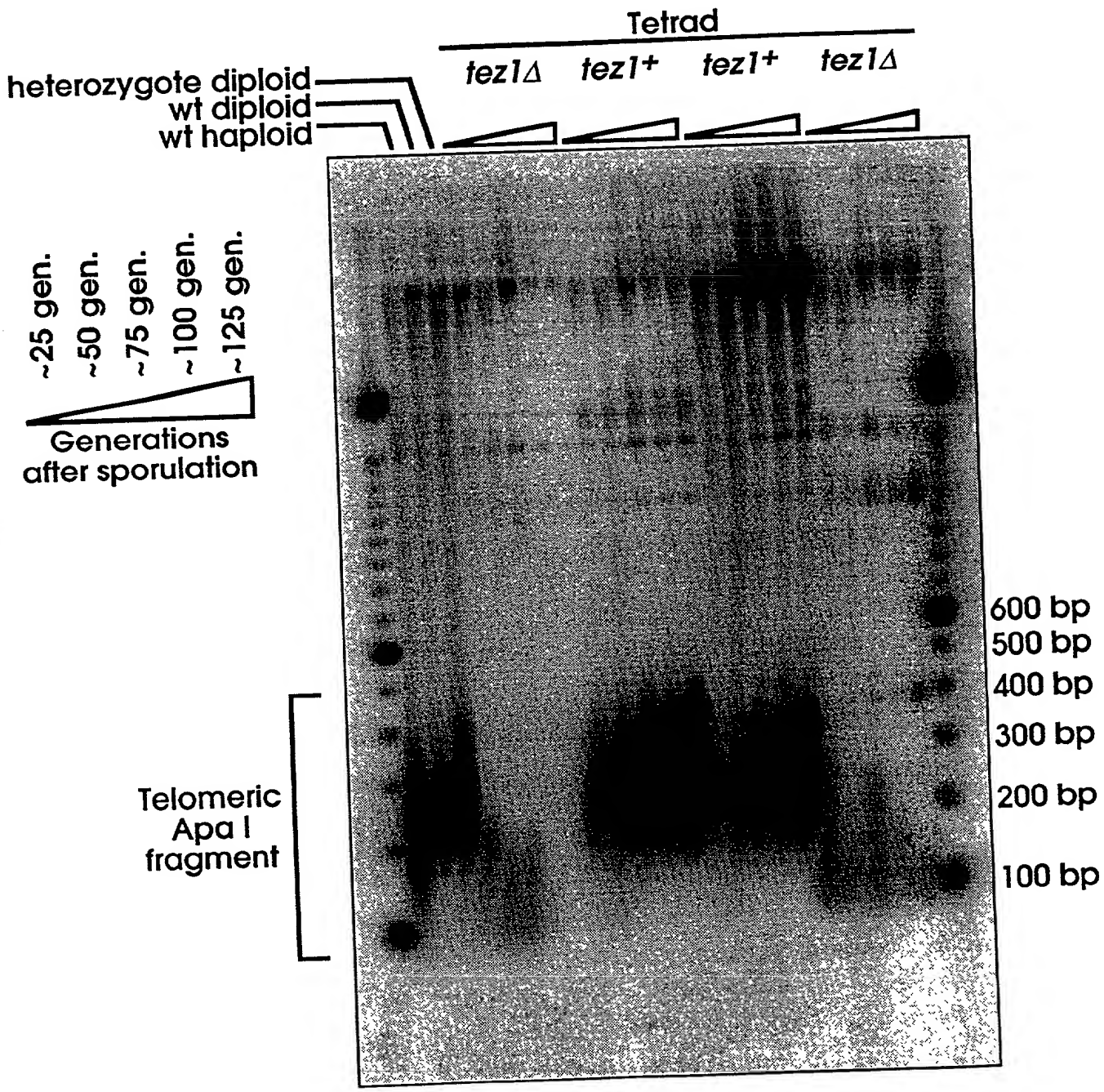

Tez1 disruption causes progressive shortening of telomeres in S. pombe
Tetrad
tez1Δ
tez1+
tez1+
tez1Δ
heterozygote diploid
wt diploid
wt haploid
~25 gen.
~50 gen.
~75 gen.
~100 gen.
~125 gen.
Generations after sporulation
600 bp
500 bp
400 bp
300 bp
200 bp
100 bp
Telomeric Apa I fragment

FIGURE 46

```
1 ggtaccgatttactttcctttcttcataagctaattgcttcctcgaacgctcctaaatctctggaaatatttttacaaga 80
81 actcaataacaataccaagtcaaattccaatatgaaggtgttattagtgatcgataatatttctattttatcggtcgtta 160
161 ccaagtataaggacaaaaagaacaacttccttccccctaaagacttttacttttattaatttacttttcaaatatatttcg 240
241 ggttcgcttacttttaatcgtggtactgttttagctgctacttctagccaaccgcgtgtttctaccccgtcattggatat 320
321 agctcttggagtagctcacagaaatccttacaaatcttctgatgagactatattagattcattacagtccgtgcatattc 400
401 ttaacatggagccttacactttagatgagtcacgtcgcatgatggagtatttggtatcatccaacgtttgccttgaaaag 480
481 gttgataattatttgcaaaatcatgtccttagtggtggtaatccgcgaaagtttttgatgcttgcacacgtctagcatg 560
561 attgagatattcaaaaatttctatccactacaactcctttaacgcggttttatttttctattttctattctcatgttgtt 640
641 ccaaatatgtatcatctcgtattaggctttttccgttttactcctggaatcgtacctttttcactattccccctaatga 720
721 ataatctaaattagtttcgcttataattgatagtagtagaaagattggtgattctactcgtgtaatgttattagtttaaa 800
801 gatactttgcaaaacatttattagctatcattatataaaaaaaatcctataattataaatattaatcaatatttgcggtc 880
881 actatttatttaaaacgttatgatcagtaggacactttgcatatatatagttatgcttaatggttacttgtaacttgc 958

959 ATG ACC GAA CAC CAT ACC CCC AAA AGC AGG ATT CTT CGC TTT CTA GAG AAT CAA TAT GTA 1018
  1 M   T   E   H   H   T   P   K   S   R   I   L   R   F   L   E   N   Q   Y   V  20

1019 TAC CTA TGT ACC TTA AAT GAT TAT GTA CAA CTT GTT TTG AGA GGG TCG CCG GCA AGC TCG 1078
 21 Y   L   C   T   L   N   D   Y   V   Q   L   V   L   R   G   S   P   A   S   S  40

1079 TAT AGC AAT ATA TGC GAA CGC TTG AGA AGC GAT GTA CAA ACG TCC TTT TCT ATT TTT CTT 1138
 41 Y   S   N   I   C   E   R   L   R   S   D   V   Q   T   S   F   S   I   F   L  60

1139 CAT TCG ACT GTA GTC GGC TTC GAC AGT AAG CCA GAT GAA GGT GTT CAA TTT TCT TCT CCA 1198
 61 H   S   T   V   V   G   F   D   S   K   P   D   E   G   V   Q   F   S   S   P  80
```

FIGURE 46 (cont.)

```
1199 AAA TGC TCA CAG TCA GAG gtatatatattttgttttgatttttttctattcgggatagctaatatatgggcag 1272
  81 K   C   S   Q   S   E                                                           86

1273 CTA ATA GCG AAT GTT GTA AAA CAG ATG TTC GAT GAA AGT TTT GAG CGT CGA AGG AAT CTA  1332
  87 L   I   A   N   V   V   K   Q   M   F   D   E   S   F   E   R   R   R   N   L    106

1333 CTG ATG AAA GGG TTT TCC ATG gtaaggtattctaattgtgaaatatttacctgcaattactgtttcaaagaga 1405
 107 L   M   K   G   F   S   M                                                       113

1406 ttgtatttaaccgataaag AAT CAT GAA GAT TTT CGA GCC ATG CAT GTA AAC GGA GTA CAA AAT  1469
 114                     N   H   E   D   F   R   A   M   H   V   N   G   V   Q   N    128

1470 GAT CTC GTT TCT ACT TTT CCT AAT TAC CTT ATA TCT ATA CTT GAG TCA AAA AAT TGG CAA  1529
 129 D   L   V   S   T   F   P   N   Y   L   I   S   I   L   E   S   K   N   W   Q    148

1530 CTT TTG TTA GAA AT gtaaataccggttaagatgttgcgcactttgaacaagactgacaagtatag T ATC GGC 1601
 149 L   L   L   E   I                                                       I   G    155

1602 AGT GAT GCC ATG CAT TAC TTA TTA TCC AAA GGA AGT ATT TTT GAG GCT CTT CCA AAT GAC  1661
 156 S   D   A   M   H   Y   L   L   S   K   G   S   I   F   E   A   L   P   N   D    175

1662 AAT TAC CTT CAG ATT TCT GGC ATA CCA CTT TTT AAA AAT AAT GTG TTT GAG GAA ACT GTG  1721
 176 N   Y   L   Q   I   S   G   I   P   L   F   K   N   N   V   F   E   E   T   V    195

1722 TCA AAA AAA AGA AAG CGA ACC ATT GAA ACA TCC ATT ACT CAA AAT AAA AGC GCC CGC AAA  1781
 196 S   K   K   R   K   R   T   I   E   T   S   I   T   Q   N   K   S   A   R   K    215

1782 GAA GTT TCC TGG AAT AGC ATT TCA ATT AGT AGG TTT AGC ATT TTT TAC AGG TCA TCC TAT  1841
 216 E   V   S   W   N   S   I   S   I   S   R   F   S   I   F   Y   R   S   S   Y    235

1842 AAG AAG TTT AAG CAA G gtaactaatactgttatccttcataactaattttag AT CTA TAT TTT AAC
1907
 236 K   K   F   K   Q   D                                                   L   Y   F   N      245

1908 TTA CAC TCT ATT TGT GAT CGG AAC ACA GTA CAC ATG TGG CTT CAA TGG ATT TTT CCA AGG  1967
 246 L   H   S   I   C   D   R   N   T   V   H   M   W   L   Q   W   I   F   P   R    265

1968 CAA TTT GGA CTT ATA AAC GCA TTT CAA GTG AAG CAA TTG CAC AAA GTG ATT CCA CTG GTA  2027
 266 Q   F   G   L   I   N   A   F   Q   V   K   Q   L   H   K   V   I   P   L   V    285

2028 TCA CAG AGT ACA GTT GTG CCC AAA CGT CTC CTA AAG GTA TAC CCT TTA ATT GAA CAA ACA  2087
 286 S   Q   S   T   V   V   P   K   R   L   L   K   V   Y   P   L   I   E   Q   T    305

2088 GCA AAG CGA CTC CAT CGT ATT TCT CTA TCA AAA GTT TAC AAC CAT TAT TGC CCA TAT ATT  2147
 306 A   K   R   L   H   R   I   S   L   S   K   V   Y   N   H   Y   C   P   Y   I    325

2148 GAC ACC CAC GAT GAT GAA AAA ATC CTT AGT TAT TCC TTA AAG CCG AAC CAG GTG TTT GCG  2207
 326 D   T   H   D   D   E   K   I   L   S   Y   S   L   K   P   N   Q   V   F   A    345

2208 TTT CTT CGA TCC ATT CTT GTT CGA GTG TTT CCT AAA TTA ATC TGG GGT AAC CAA AGG ATA  2267
 346 F   L   R   S   I   L   V   R   V   F   P   K   L   I   W   G   N   Q   R   I    365

2268 TTT GAG ATA ATA TTA AAA G gtattgtataaaatttattaccactaacgattttaccag AC CTC GAA ACT 2336
 366 F   E   I   I   L   K   D                                               L   E   T    375
```

FIGURE 46 (cont.)

```
2337 TTC TTG AAA TTA TCG AGA TAC GAG TCT TTT AGT TTA CAT TAT TTA ATG AGT AAC ATA AAG 2396
 376 F   L   K   L   S   R   Y   E   S   F   S   L   H   Y   L   M   S   N   I   K   395

2397 gtaatatgccaaatttttttaccattaattaacaatcag ATT TCA GAA ATT GAA TGG CTA GTC CTT GGA 2465
 396                                        I   S   E   I   E   W   L   V   L   G   405

2466 AAA AGG TCA AAT GCG AAA ATG TGC TTA AGT GAT TTT GAG AAA CGC AAG CAA ATA TTT GCG 2525
 406 K   R   S   N   A   K   M   C   L   S   D   F   E   K   R   K   Q   I   F   A   425

2526 GAA TTC ATC TAC TGG CTA TAC AAT TCG TTT ATA ATA CCT ATT TTA CAA TCT TTT TTT TAT 2585
 426 E   F   I   Y   W   L   Y   N   S   F   I   I   P   I   L   Q   S   F   F   Y   445

2586 ATC ACT GAA TCA AGT GAT TTA CGA AAT CGA ACT GTT TAT TTT AGA AAA GAT ATT TGG AAA 2645
 446 I   T   E   S   S   D   L   R   N   R   T   V   Y   F   R   K   D   I   W   K   465

2646 CTC TTG TGC CGA CCC TTT ATT ACA TCA ATG AAA ATG GAA GCG TTT GAA AAA-ATA AAC GAG 2705
 466 L   L   C   R   P   F   I   T   S   M   K   M   E   A   F   E   K   I   N   E   485

2706 gtattttaaagtatttttttgcaaaaagctaatattttcag AAC AAT GTT AGG ATG GAT ACT CAG AAA ACT 2775
 486                                          N   N   V   R   M   D   T   Q   K   T   495

2776 ACT TTG CCT CCA GCA GTT ATT CGT CTA TTA CCT AAG AAG AAT ACC TTT CGT CTC ATT ACG 2835
 496 T   L   P   P   A   V   I   R   L   L   P   K   K   N   T   F   R   L   I   T   515

2836 AAT TTA AGA AAA AGA TTC TTA ATA AAG gtattaatttttggtcatcaatgtactttacttctaatctatta 2906
 516 N   L   R   K   R   F   L   I   K                                                524

2907 ttagcag ATG GGT TCA AAC AAA AAA ATG TTA GTC AGT ACG AAC CAA ACT TTA CGA CCT GTG 2967
 525         M   G   S   N   K   K   M   L   V   S   T   N   Q   T   L   R   P   V   542

2968 GCA TCG ATA CTG AAA CAT TTA ATC AAT GAA GAA AGT AGT GGT ATT CCA TTT AAC TTG GAG 3027
 543 A   S   I   L   K   H   L   I   N   E   E   S   S   G   I   P   F   N   L   E   562

3028 GTT TAC ATG AAG CTT CTT ACT TTT AAG AAG GAT CTT CTT AAG CAC CGA ATG TTT GG gtaat 3088
 563 V   Y   M   K   L   L   T   F   K   K   D   L   L   K   H   R   M   F   G       581

3089 tatataatgcgcgattcctcattattaattttgcag G CGT AAG AAG TAT TTT GTA CGG ATA GAT ATA   3155
 582                                      R   K   K   Y   F   V   R   I   D   I     591

3156 AAA TCC TGT TAT GAT CGA ATA AAG CAA GAT TTG ATG TTT CGG ATT GTT AAA AAG AAA CTC 3215
 592 K   S   C   Y   D   R   I   K   Q   D   L   M   F   R   I   V   K   K   K   L   611

3216 AAG GAT CCC GAA TTT GTA ATT CGA AAG TAT GCA ACC ATA CAT GCA ACA AGT GAC CGA GCT 3275
 612 K   D   P   E   F   V   I   R   K   Y   A   T   I   H   A   T   S   D   R   A   631

3276 ACA AAA AAC TTT GTT AGT GAG GCG TTT TCC TAT T gtaagtttatttttttcattggaatttttttaacaa 3343
 632 T   K   N   F   V   S   E   A   F   S   Y   F                                    643

3344 attctttttttag TT GAT ATG GTG CCT TTT GAA AAA GTC GTG CAG TTA CTT TCT ATG AAA ACA 3405
 644               D   M   V   P   F   E   K   V   V   Q   L   L   S   M   K   T   659

3406 TCA GAT ACT TTG TTT GTT GAT TTT GTG GAT TAT TGG ACC AAA AGT TCT TCT GAA ATT TTT 3465
 660 S   D   T   L   F   V   D   F   V   D   Y   W   T   K   S   S   S   E   I   F   679

3466 AAA ATG CTC AAG GAA CAT CTC TCT GGA CAC ATT GTT AAG gtataccaattgttgaattgtaataaca 3532
 680 K   M   L   K   E   H   L   S   G   H   I   V   K                                692
```

FIGURE 46 (cont.)

```
3533 ctaatgaaactag ATA GGA AAT TCT CAA TAC CTT CAA AAA GTT GGT ATC CCT CAG GGC TCA    3593
 693              I   G   N   S   Q   Y   L   Q   K   V   G   I   P   Q   G   S     708

3594 ATT CTG TCA TCT TTT TTG TGT CAT TTC TAT ATG GAA GAT TTG ATT GAT GAA TAC CTA TCG 3653
 709 I   L   S   S   F   L   C   H   F   Y   M   E   D   L   I   D   E   Y   L   S   728

3654 TTT ACG AAA AAG AAA GGA TCA GTG TTG TTA CGA GTA GTC GAC GAT TTC CTC TTT ATA ACA 3713
 729 F   T   K   K   K   G   S   V   L   L   R   V   V   D   D   F   L   F   I   T   748

3714 GTT AAT AAA AAG GAT GCA AAA AAA TTT TTG AAT TTA TCT TTA AGA G gtgagttgctgtcattcc 3777
 749 V   N   K   K   D   A   K   K   F   L   N   L   S   L   R   G                   764

3778 taagttctaaccgttgaag GA TTT GAG AAA CAC AAT TTT TCT ACG AGC CTG GAG AAA ACA GTA   3840
 765                       F   E   K   H   N   F   S   T   S   L   E   K   T   V     778

3841 ATA AAC TTT GAA AAT AGT AAT GGG ATA ATA AAC AAT ACT TTT TTT AAT GAA AGC AAG AAA 3900
 779 I   N   F   E   N   S   N   G   I   I   N   N   T   F   F   N   E   S   K   K   798

3901 AGA ATG CCA TTC TTC GGT TTC TCT GTG AAC ATG AGG TCT CTT GAT ACA TTG TTA GCA TGT 3960
 799 R   M   P   F   F   G   F   S   V   N   M   R   S   L   D   T   L   L   A   C   818

3961 CCT AAA ATT GAT GAA GCC TTA TTT AAC TCT ACA TCT GTA GAG CTG ACG AAA CAT ATG GGG 4020
 819 P   K   I   D   E   A   L   F   N   S   T   S   V   E   L   T   K   H   M   G   838

4021 AAA TCT TTT TTT TAC AAA ATT CTA AG gtatactgtgtaactgaataatagctgacaaataatcag A TCG 4089
 839 K   S   F   F   Y   K   I   L   R                                           S   848

4090 AGC CTT GCA TCC TTT GCA CAA GTA TTT ATT GAC ATT ACC CAC AAT TCA AAA TTC AAT TCT 4149
 849 S   L   A   S   F   A   Q   V   F   I   D   I   T   H   N   S   K   F   N   S   868

4150 TGC TGC AAT ATA TAT AGG CTA GGA TAC TCT ATG TGT ATG AGA GCA CAA GCA TAC TTA AAA 4209
 869 C   C   N   I   Y   R   L   G   Y   S   M   C   M   R   A   Q   A   Y   L   K   888

4210 AGG ATG AAG GAT ATA TTT ATT CCC CAA AGA ATG TTC ATA ACG G gtgagtacttattttaactaga 4274
 889 R   M   K   D   I   F   I   P   Q   R   M   F   I   T   D                       903

4275 aaagtcattaattaaccttag AT CTT TTG AAT GTT ATT GGA AGA AAA ATT TGG AAA AAG TTG GCC 4339
 904                       L   L   N   V   I   G   R   K   I   W   K   K   L   A   917

4340 GAA ATA TTA GGA TAT ACG AGT AGG CGT TTC TTG TCC TCT GCA GAA GTC AAA TG gtacgtgtc 4401
 918 E   I   L   G   Y   T   S   R   R   F   L   S   S   A   E   V   K   W           935

4402 ggtctcgagacttcagcaatattgacacatcag G CTT TTT TGT CTT GGA ATG AGA GAT GGT TTG AAA 4468
 936                                   L   F   C   L   G   M   R   D   G   L   K   946

4469 CCC TCT TTC AAA TAT CAT CCA TGC TTC GAA CAG CTA ATA TAC CAA TTT CAG TCA TTG ACT 4528
 947 P   S   F   K   Y   H   P   C   F   E   Q   L   I   Y   Q   F   Q   S   L   T   966

4529 GAT CTT ATC AAG CCG CTA AGA CCA GTT TTG CGA CAG GTG TTA TTT TTA CAT AGA AGA ATA 4588
 967 D   L   I   K   P   L   R   P   V   L   R   Q   V   L   F   L   H   R   R   I   986

4589 GCT GAT TAA tgtcattttcaatttattatatacatcctttattactggtgtcttaaacaatattattactaagtata 4665
 987 A   D   *                                                                       989
```

FIGURE 46 (cont.)

```
4666 gctgacccccaaagcaagcatactataggatttctagtaaagtaaaattaatctcgttattagttttgattgacttgtct 4745
4746 ttatccttatacttttaagaaagattgacagtggttgctgactactgcccacatgcccattaaacgggagtggttaaaca 4825
4826 ttaaaagtaatacatgaggctaatctcctttcatttagaataaggaaagtggttttctataatgaataatgcccgcacta 4905
4906 atgcaaaaagacgaagattatcttctaaacaagggggattaagcatatccgaaggaaaagagagtaatatacccagtgtt 4985
4986 gttgaagaaagcaaggataatttggaacaagcttctgcagatgacaggctaaattttggtgaccgaattttggtaaaagc 5065
5066 cccaggttatccatggtggccggccttgctactgagacgaaaagaaactaaggatagtttgaatactaatagctcattta 5145
5146 atgtcttatataaggttttgtttttcctgacttcaattttgcatgggtgaaaagaaatagtgttaagccattattggat 5225
5226 tccgaaatagccaaatttcttggttcctcaaagcggaagtctaaagaacttattgaagcttatgaggcttcaaaaactcc 5305
5306 tcctgatttaaaggaggaatcttccaccgatgaggaaatggatagcttatcagctgctgaggagaagcctaatttttgc 5385
5386 aaaaaagaaaatatcattgggagacatctcttgatgaatcagatgcggagagtatctccagcggatccttgatgtcaata 5465
5466 acttctatttctgaaatgtatggtcctactgtcgcttcgacttctcgtagctctacgcagttaagtgaccaaaggtacc  5544
```

FIGURE 47

```
                                1
                               met ser val tyr val val glu leu leu
GCCAAGTTCCTGCACTGGCTG          ATG AGT GTG TAC GTC GTC GAG CTG CTC

 10                                                  20
arg ser phe phe tyr val thr glu thr thr phe gln lys asn arg
AGG TCT TTC TTT TAT GTC ACG GAG ACC ACG TTT CAA AAG AAC AGG

                           30
leu phe phe tyr arg lys ser val trp ser lys leu gln ser ile
CTC TTT TTC TAC CGG AAG AGT GTC TGG AGC AAG TTG CAA AGC ATT

 40                                                  50
gly ile arg gln his leu lys arg val gln leu arg glu leu ser
GGA ATC AGA CAG CAC TTG AAG AGG GTG CAG CTG CGG GAG CTG TCG

                           60
glu ala glu val arg gln his arg glu ala arg pro ala leu leu
GAA GCA GAG GTC AGG CAG CAT CGG GAA GCC AGG CCC GCC CTG CTG

 70                                                  80
thr ser arg leu arg phe ile pro lys pro asp gly leu arg pro
ACG TCC AGA CTC CGC TTC ATC CCC AAG CCT GAC GGG CTG CGG CCG

                           90
ile val asn met asp tyr val val gly ala arg thr phe arg arg
ATT GTG AAC ATG GAC TAC GTC GTG GGA GCC AGA ACG TTC CGC AGA

100                                                 110
glu lys      ala glu arg leu thr ser arg val lys ala leu phe
GAA AAG ARG GCC GAG CGT CTC ACC TCG AGG GTG AAG GCA CTG TTC

                          120
ser val leu asn tyr glu arg ala arg arg pro gly leu leu gly
AGC GTG CTC AAC TAC GAG CGG GCG CGG CGC CCC GGC CTC CTG GGC

130                                                 140
ala ser val leu gly leu asp asp ile his arg ala trp arg thr
GCC TCT GTG CTG GGC CTG GAC GAT ATC CAC AGG GCC TGG CGC ACC

                          150
phe val leu arg val arg ala gln asp pro pro pro glu leu tyr
TTC GTG CTG CGT GTG CGG GCC CAG GAC CCG CCG CCT GAG CTG TAC

160                                                 170
phe val lys val asp val thr gly ala tyr asp thr ile pro gln
TTT GTC AAG GTG GAT GTG ACG GGC GCG TAC GAC ACC ATC CCC CAG

                          180
asp arg leu thr glu val ile ala ser ile ile lys pro gln asn
GAC AGG CTC ACG GAG GTC ATC GCC AGC ATC ATC AAA CCC CAG AAC
```

FIGURE 47 (cont.)

```
190                                         200
thr tyr cys val arg arg tyr ala val val gln lys ala ala met
ACG TAC TGC GTG CGT CGG TAT GCC GTG GTC CAG AAG GCC GCC ATG

                     210
gly thr ser ala arg pro ser arg ala thr ser tyr val gln cys
GGC ACG TCC GCA AGG CCT TCA AGA GCC ACG TCC TAC GTC CAG TGC

220                                         230
gln gly ile pro gln gly ser ile leu ser thr leu leu cys ser
CAG GGG ATC CCG CAG GGC TCC ATC CTC TCC ACG CTG CTC TGC AGC

                     240
leu cys tyr gly asp met glu asn lys leu phe ala gly ile arg
CTG TGC TAC GGC GAC ATG GAG AAC AAG CTG TTT GCG GGG ATT CGG

250                                         260
arg asp gly leu leu leu arg leu val asp asp phe leu leu val
CGG GAC GGG CTG CTC CTG CGT TTG GTG GAT GAT TTC TTG TTG GTG

                     270
thr pro his leu thr his ala lys thr phe leu arg thr leu val
ACA CCT CAC CTC ACC CAC GCG AAA ACC TTC CTC AGG ACC CTG GTC

280                                         290
arg gly val pro glu tyr gly cys val val asn leu arg lys thr
CGA GGT GTC CCT GAG TAT GGC TGC GTG GTG AAC TTG CGG AAG ACA

                     300
val val asn phe pro val glu asp glu ala leu gly gly thr ala
GTG GTG AAC TTC CCT GTA GAA GAC GAG GCC CTG GGT GGC ACG GCT

310                                         320
phe val gln met pro ala his gly leu phe pro trp cys gly leu
TTT GTT CAG ATG CCG GCC CAC GGC CTA TTC CCC TGG TGC GGC CTG

                     330
leu leu asp thr arg thr leu glu val gln ser asp tyr ser ser
CTG CTG GAT ACC CGG ACC CTG GAG GTG CAG AGC GAC TAC TCC AGC

340                                         350
tyr ala arg thr ser ile arg ala ser leu thr phe asn arg gly
TAT GCC CGG ACC TCC ATC AGA GCC AGT CTC ACC TTC AAC CGC GGC

                     360
phe lys ala gly arg asn met arg arg lys leu phe gly val leu
TTC AAG GCT GGG AGG AAC ATG CGT CGC AAA CTC TTT GGG GTC TTG

370                                         380
arg leu lys cys his ser leu phe leu asp leu gln val asn ser
CGG CTG AAG TGT CAC AGC CTG TTT CTG GAT TTG CAG GTG AAC AGC
```

FIGURE 47 (cont.)

```
                    390
leu gln thr val cys thr asn ile tyr lys ile leu leu leu gln
CTC CAG ACG GTG TGC ACC AAC ATC TAC AAG ATC CTC CTG CTG CAG

400                                         410
ala tyr arg phe his ala cys val leu gln leu pro phe his gln
GCG TAC AGG TTT CAC GCA TGT GTG CTG CAG CTC CCA TTT CAT CAG

                    420
gln val trp lys asn pro his phe ser cys ala ser ser leu thr
CAA GTT TGG AAG AAC CCA CAT TTT TCC TGC GCG TCA TCT CTG ACA

430                                         440
arg leu pro leu leu leu his pro glu ser gln glu arg arg asp
CGG CTC CCT CTG CTA CTC CAT CCT GAA AGC CAA GAA CGC AGG GAT

                    450
val ala gly gly gln gly arg arg arg pro ser ala leu arg gly
GTC GCT GGG GGC CAA GGG CGC CGC CGG CCC TCT GCC CTC CGA GGC

460                                         470
arg ala val ala val pro pro ser ile pro ala gln ala asp ser
CGT GCA GTG GCT GTG CCA CCA AGC ATT CCT GCT CAA GCT GAC TCG

                    480
thr pro cys his leu arg ala thr pro gly val thr gln asp ser
ACA CCG TGT CAC CTA CGT GCC ACT CCT GGG GTC ACT CAG GAC AGC

490                                         500
pro asp ala ala glu ser glu ala pro gly asp asp ala asp cys
CCA GAC GCA GCT GAG TCG GAA GCT CCC GGG GAC GAC GCT GAC TGC

                    510
pro gly gly arg ser gln pro gly thr ala leu arg leu gln asp
CCT GGA GGC CGC AGC CAA CCC GGC ACT GCC CTC AGA CTT CAA GAC

520                                         530
his pro gly leu met ala thr arg pro gln pro gly arg glu gln
CAT CCT GGA CTG ATG GCC ACC CGC CCA CAG CCA GGC CGA GAG CAG

                    540
thr pro ala ala leu ser arg arg ala tyr thr ser gln gly gly
ACA CCA GCA GCC CTG TCA CGC CGG GCT TAT ACG TCC CAG GGA GGG

550                                         560
arg gly gly pro his pro gly leu his arg trp glu ser glu ala
AGG GGC GGC CCA CAC CCA GGC CTG CAC CGC TGG GAG TCT GAG GCC

564
OP
TGA GTGAGTGTTTGGCCGAGGCCTGCATGTCCGGCTGAAGGCTGAGTGTCCGGCTGAGGC

CTGAGCGAGTGTCCAGCCAAGGGCTGAGTGTCCAGCACACCTGCGTTTTCACTTCCCCAC
```

FIGURE 47 (cont.)

AGGCTGGCGTTCGGTCCACCCCAGGGCCAGCTTTTCCTCACCAGGAGCCCGGCTTCCACT

CCCCACATAGGAATAGTCCATCCCCAGATTCGCCATTGTTCACCCTTCGCCCTGCCTTCC

TTTGCCTTCCACCCCCACCATTCAGGTGGAGACCCTGAGAAGGACCCTGGGAGCTTTGGG

AATTTGGAGTGACCAAAGGTGTGCCCTGTACACAGGCGAGGACCCTGCACCTGGATGGGG

GTCCCTGTGGGTCAAATTGGGGGGAGGTGCTGTGGGAGTAAAATACTGAATATATGAGTT

TTTCAGTTTTGGAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 48

```
Motif -1
Ep p123      ...LVVSLIRCFFYVTEQQKSYSKT...
Sp Tez1      ...FIIPILQSFFYITESSDLRNRT...
Sc Est2      ...LIPKIIQTFFYCTEISSTVTIV...
Hs TCP1      ...YVVELLRSFFYVTETTFQKNRL...
consensus        FFY TE

                          K
Motif 0        p hhh K    hR h      R
Ep p123      ...KSLGFAPGKLRLIPKKT--TFRPIMTFNKKIV...
Sp Tez1      ...QKTTLPPAVIRLLPKKN--TFRLITNLRKRFL...
Sc Est2      ...TLSNFNHSKMRIIPKKSNNEFRILAIPCRGAD...
Hs TCP1      ...ARPALLTSRLRFIPKPD--GLRPIVNMDYVVG...
consensus          R PK     R I

                  AF
Motif A         h hDh GY h
Ep p123      ...PKLFFATMDIEKCYDSVNREKLSTFLK...
Sp Tez1      ...RKKYFVRIDIKSCYDRIKQDLMFRIVK...
Sc Est2      ...PELYFMKFDVKSCYDSIPRMECMRILK...
Hs TCP1      ...PELYFVKVDVTGAYDTIPQDRLTEVIA.../...
consensus      F  D   YD

Motif B            hPQG  pS hh
Ep p123      ...NGKFYKQTKGIPQGLCVSSILSSFYYA...
Sp Tez1      ...GNSQYLQKVGIPQGSILSSFLCHFYME...
Sc Est2      ...EDKCYIREDGLFQGSSLSAPIVDLVYD...
Hs TCP1      ...RATSYVQCQGIPQGSILSTLLCSLCYG...
consensus          G QG  S

                 Y
Motif C         h F DDhhh
Ep p123      ...PNVNLLMRLTDDYLLITTQENN...

Sp Tez1      ...KKGSVLLRVVDDFLFITVNKKD...
Sc Est2      ...SQDTLILKLADDFLIISTDQQQ...
Hs TCP1      ...RRDGLLLRLVDDFLLVTPHLTH...
consensus          DD L

Motif D         Gh h cK
Ep p123      ...NVSRENGFKFNMKKL...
Sp Tez1      ...LNLSLRGFEKHNFST...
Sc Est2      ...KKLAMGGFQKYNAKA...
Hs TCP1      ...LRTLVRGVPEYGCVV...
consensus        G
```